

Chart showing the major contributing factors in the progression of Coronary Heart Disease (CHD) and how the activity of cocoa procyanidins contributes to the prevention of the progression of the disease state

FIG.2 a

The cocoa procyanidins induce the activity of NOS and therefor the resulting production NO, thereby enhancing the health benefits mediated by the activity of nitric oxide (NO).

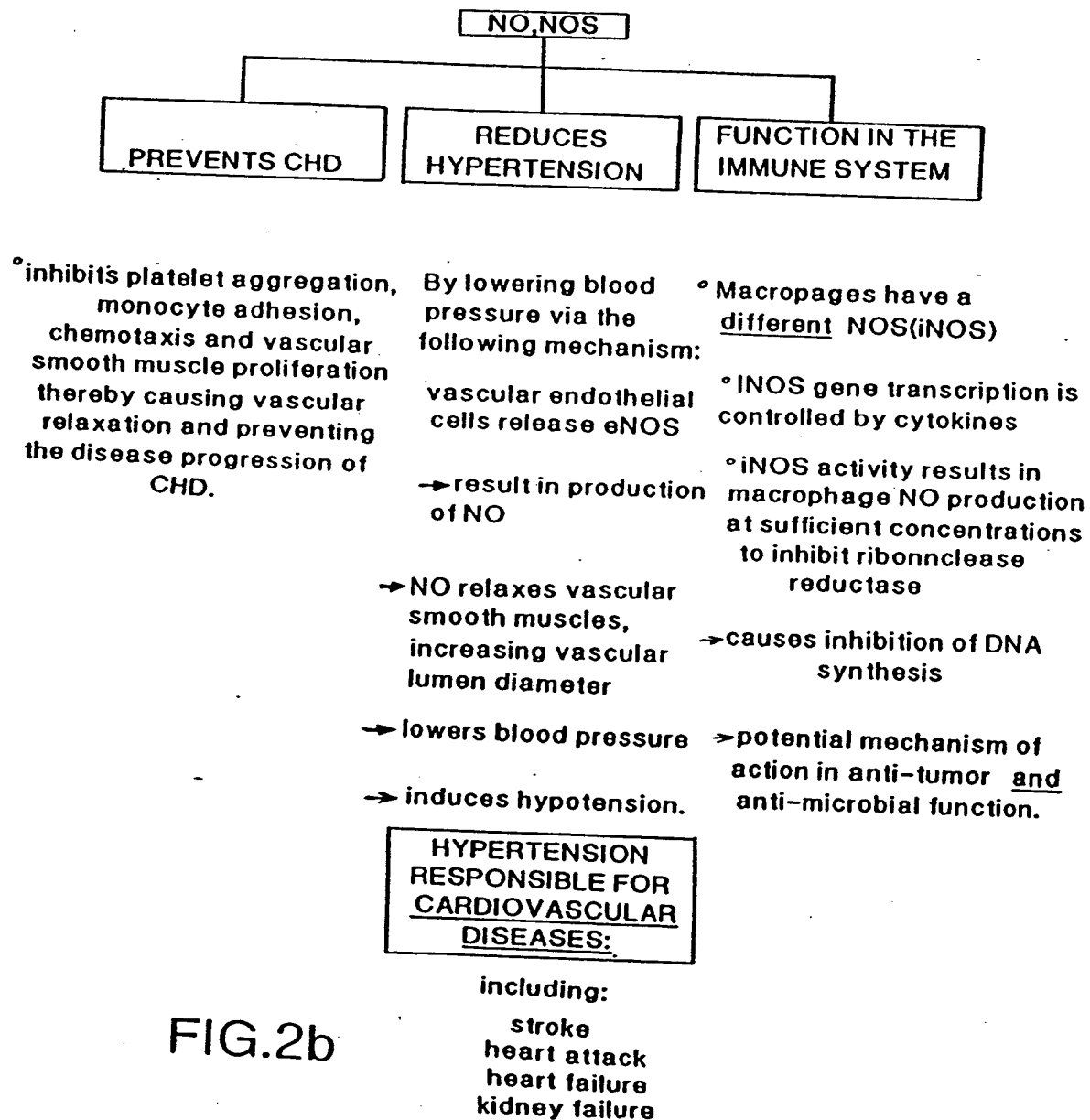
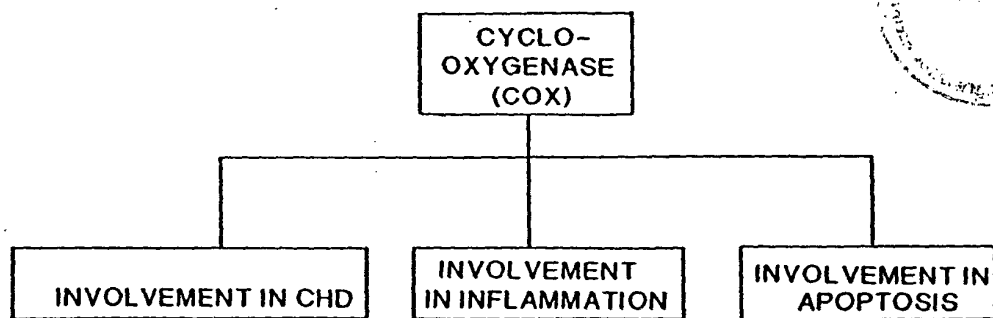


FIG.2b



COX-1 is essential in the arachidonic acid pathway which results in the production of thromboxane.

→ thromboxane and prostaglandins which promote platelet aggregation and vasoconstriction

→ resulting in progression of atherosclerosis.

COX-1 is an essential enzyme in the inflammatory pathway, the penultimate products of which (the

prostaglandins) are largely responsible for the inflammatory pathway, the results of which contribute to a variety of diseases including:

→ bowel disease, arthritis, edema, gingivitis/periodontitis, etc.

COX-2 producing cells lines show enhanced expression of genes known to be involved in apoptosis:

→ potential putative mechanism of killing tumor cells.

The cocoa procyanidins inhibit the production of cyclo-oxygenase, thereby blocking the arachidonic acid pathway, which is responsible for the inflammatory response and the vasoconstrictive and platelet aggregating responses which contribute to the disease progression of CHD.

FIG.2c



FIG.4

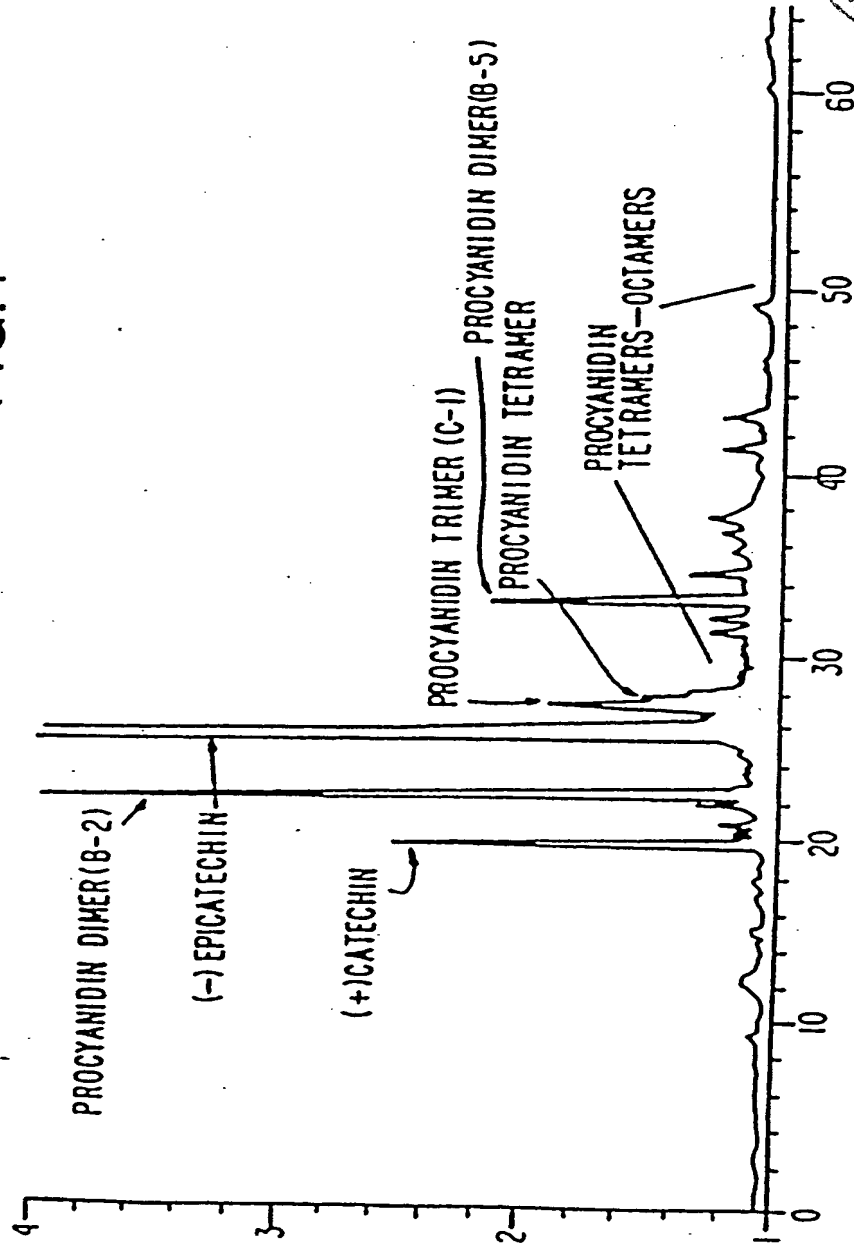


FIG.5

DADI A, Sig=280,4 Ref=580,4001 4078/009-0401.D

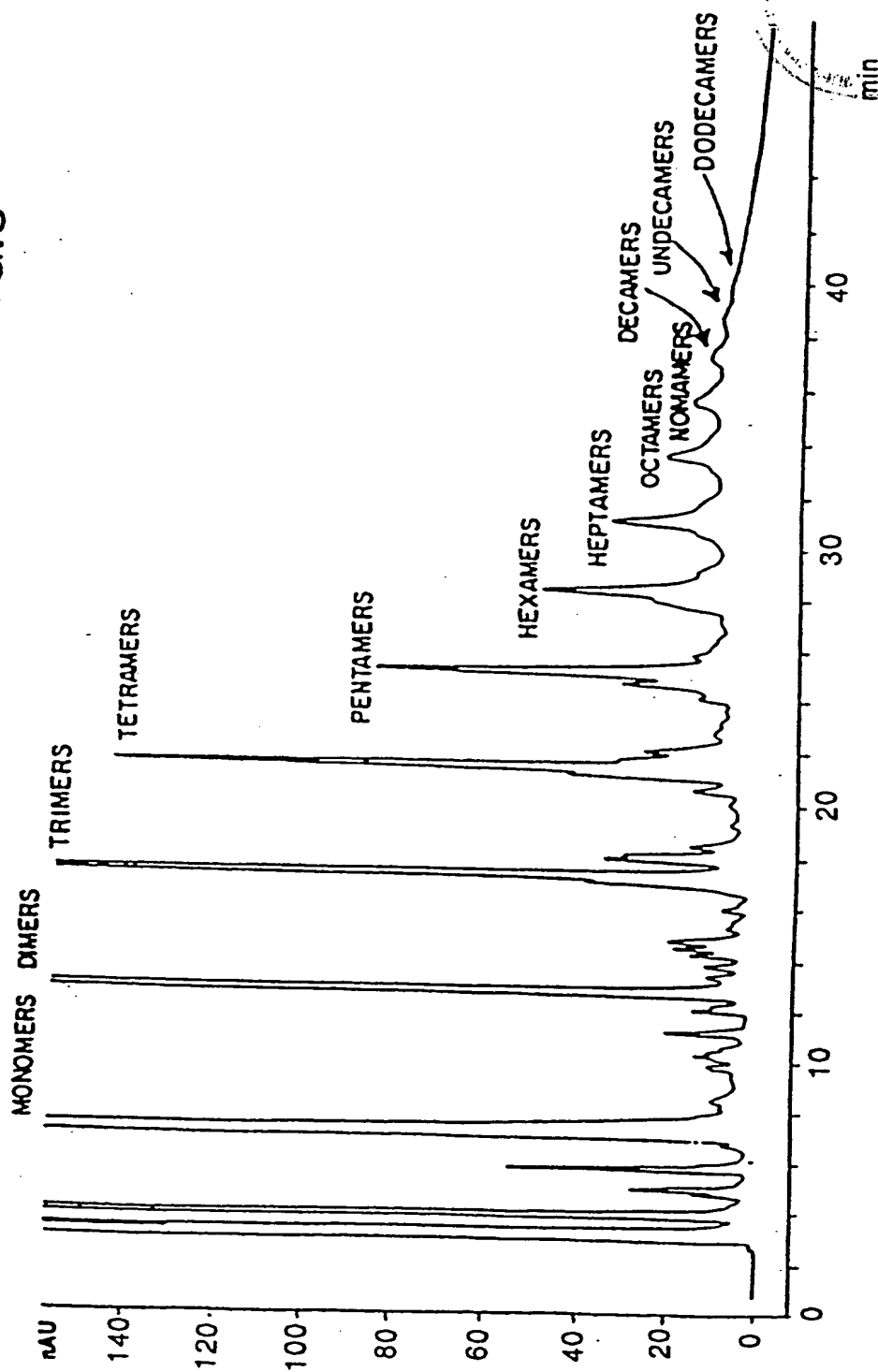
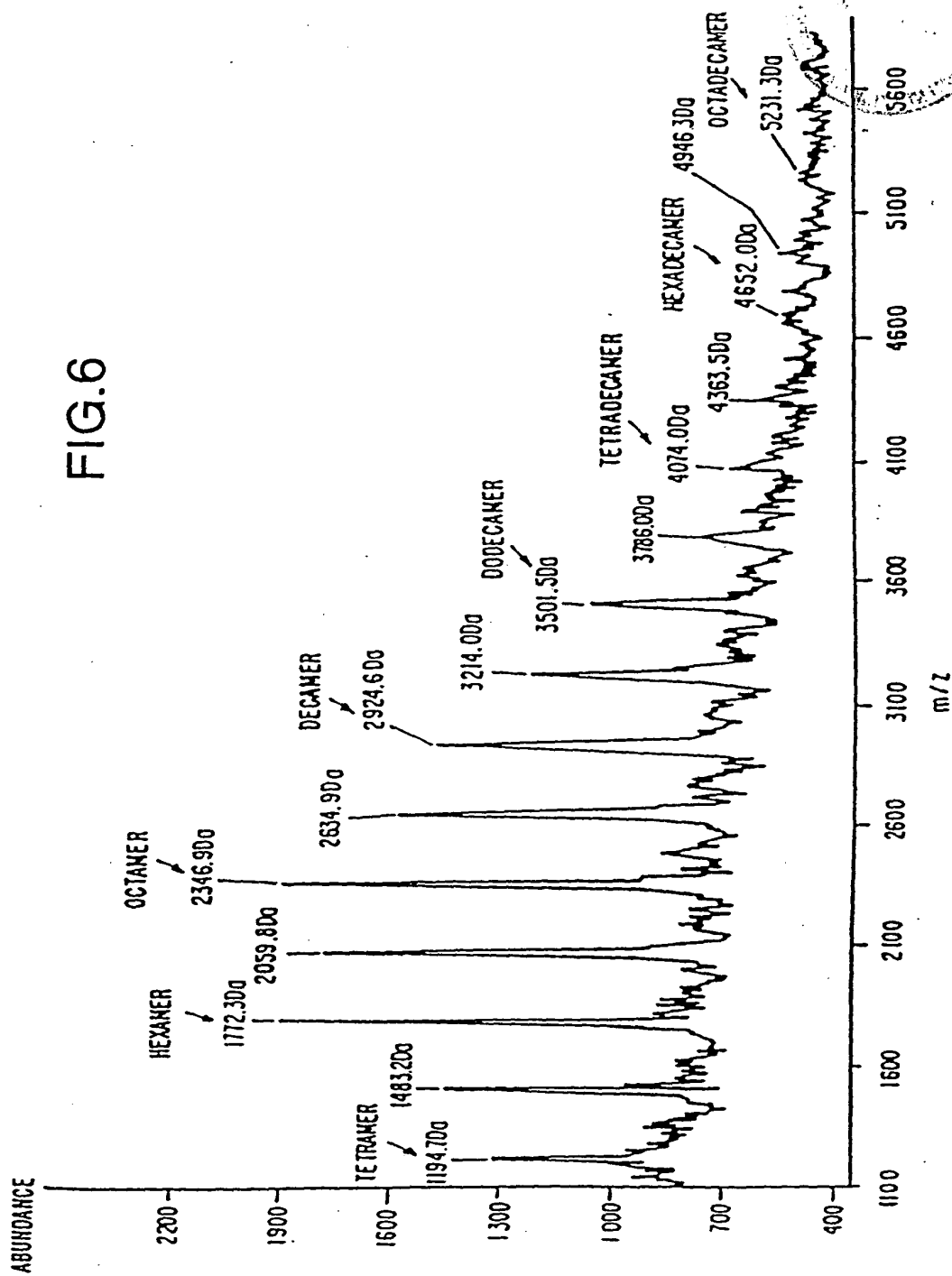


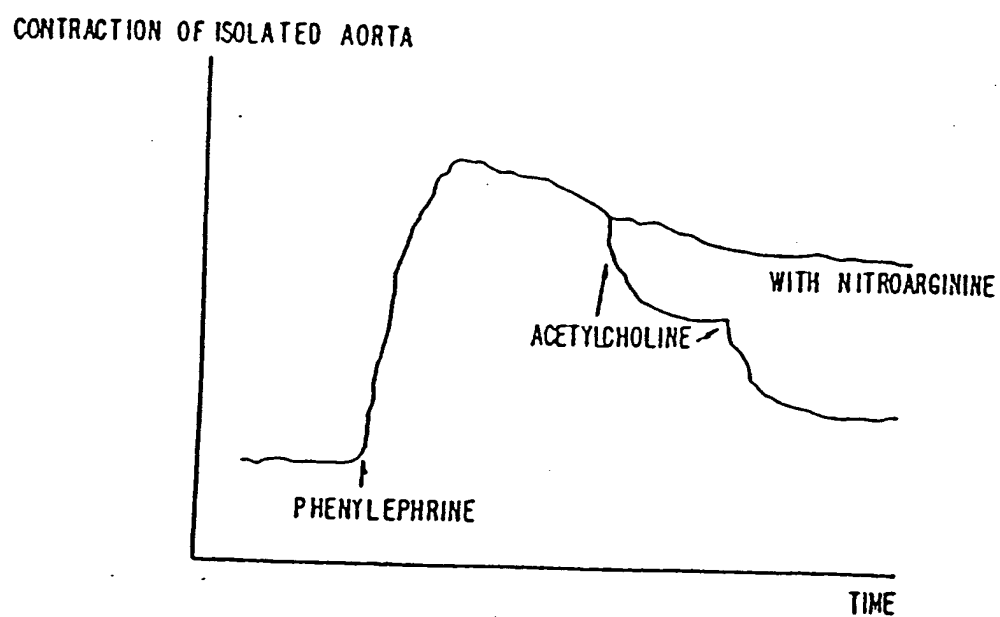
FIG. 6



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FIG.7

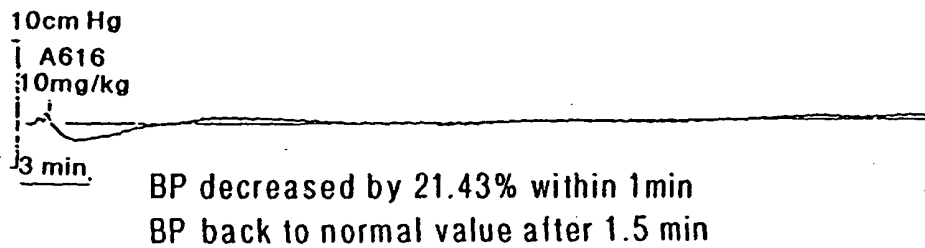


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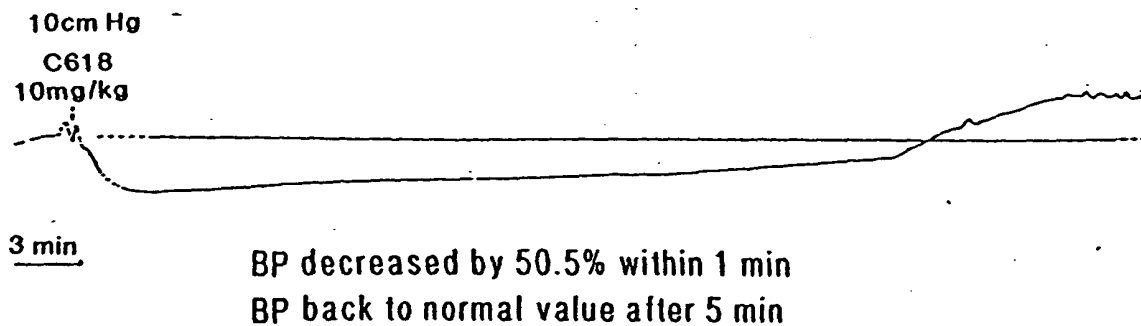
## FIG.8A

EFFECT OF COCOA PROCYANIDIN FRACTION A ON  
BLOOD PRESSURE



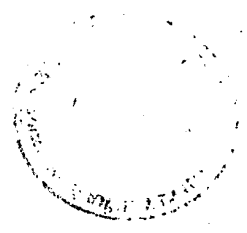
## FIG.8B

EFFECT OF COCOA PROCYANIDIN FRACTION C ON  
BLOOD PRESSURE

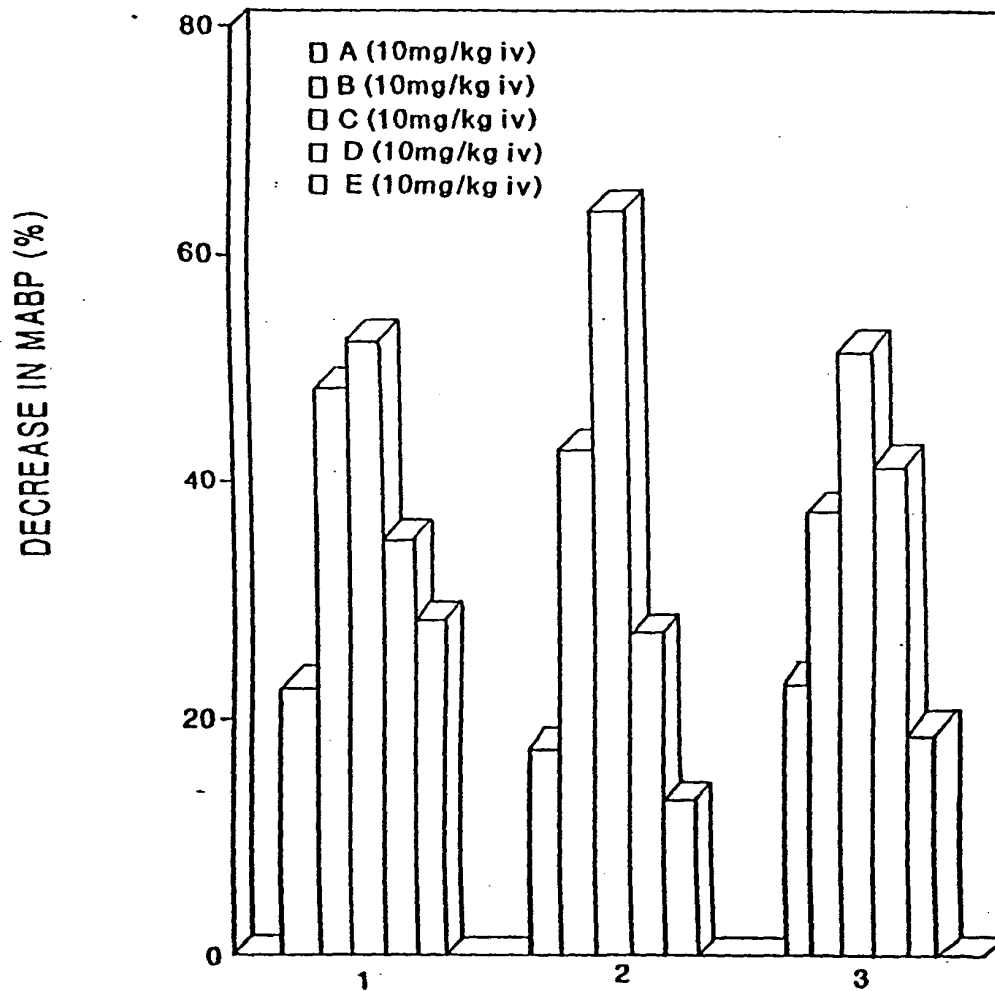




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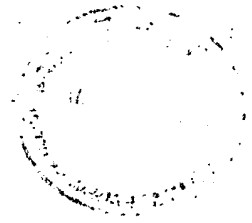
EFFECT OF COCOA PROCYANIDIN FRACTIONS ON ARTERIAL  
BLOOD PRESSURE IN ANESTHESIZED GUINEA PIGS



ASSAY

FIG.9

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EFFECT OF L-NMMA ON THE ALTERATIONS OF ARTERIAL  
BLOOD PRESSURE IN ANESTHESIZED GUINEA PIGS INDUCED BY  
COCOA PROCYANIDIN FRACTION C

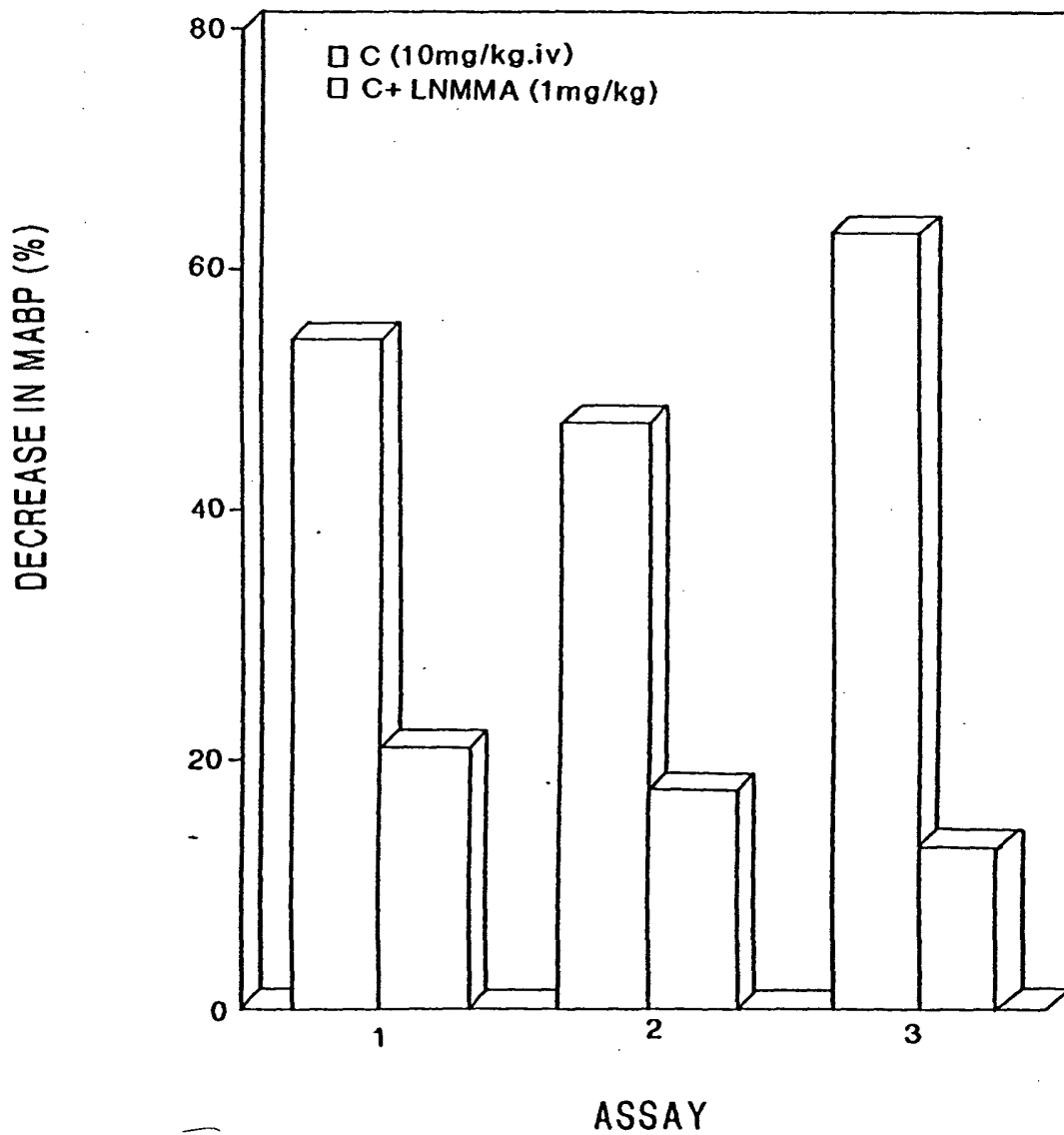
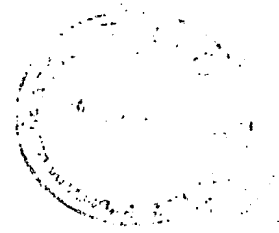


FIG.10



## EFFECT OF BRADYKININ ON NO PRODUCTION BY HUVEC

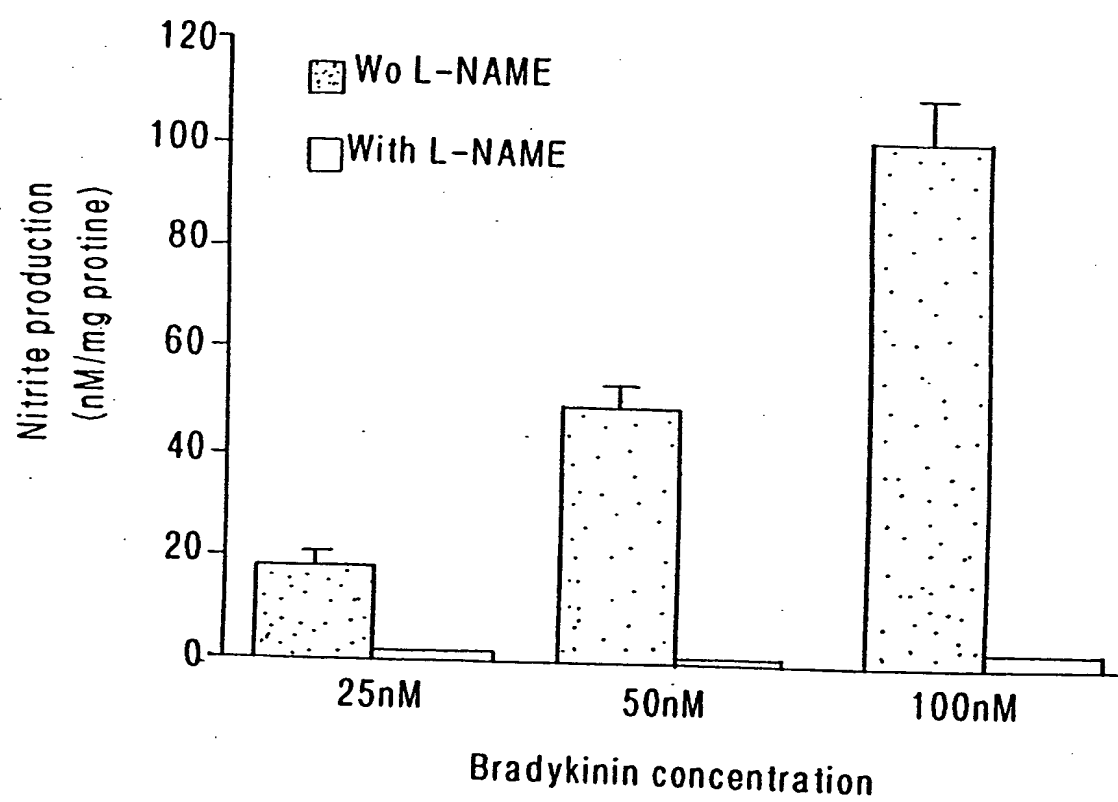
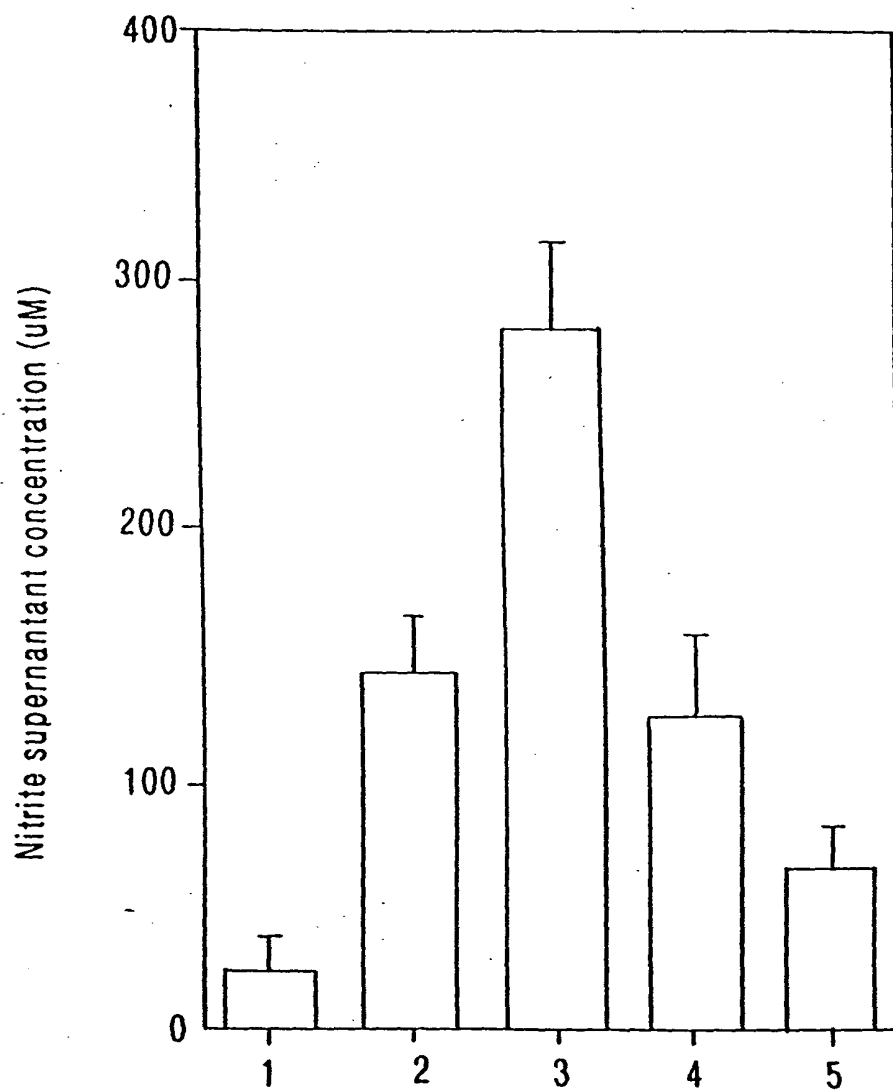


FIG.11

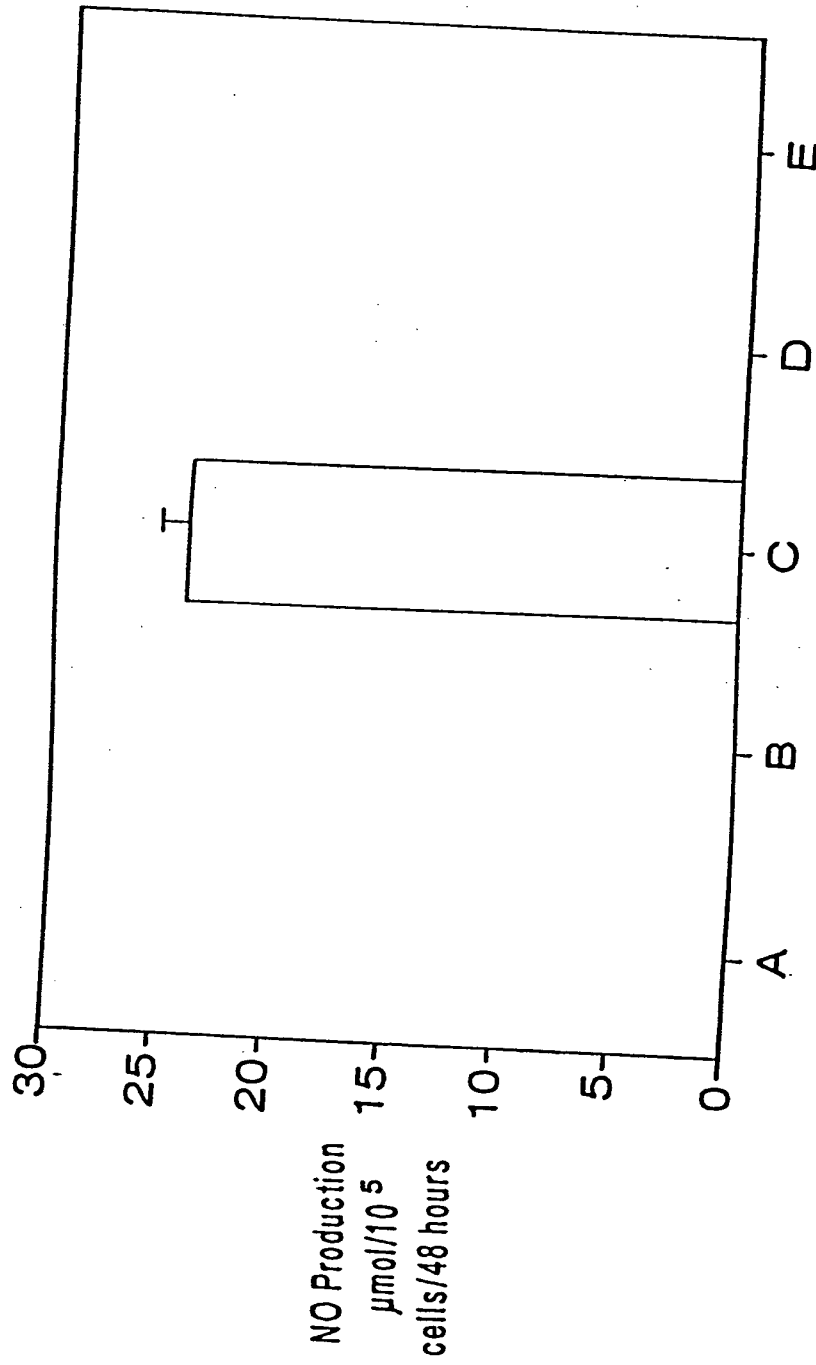
EFFECT OF COCOA PROCYANIDIN FRACTIONS ON NO  
PRODUCTION BY HUVEC



Samples A,B,D and E  
(mean of 3 assays)

FIG.12

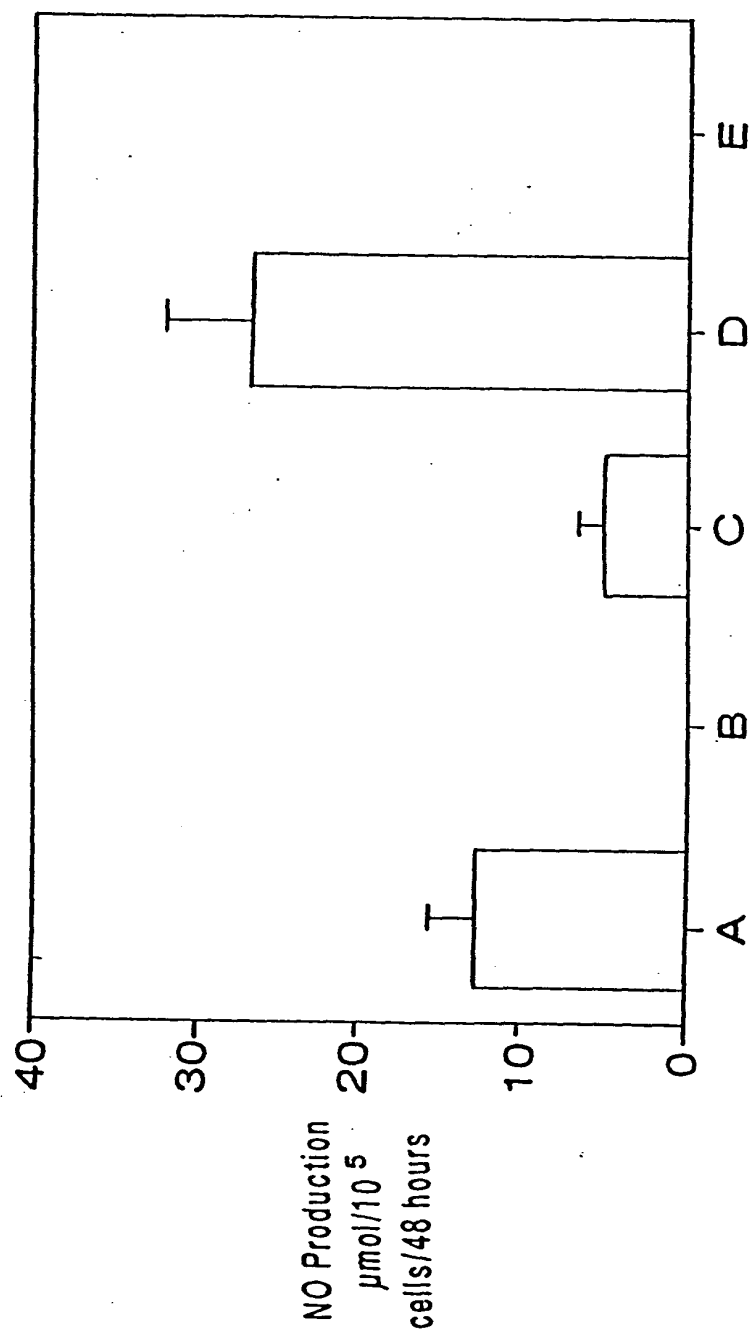
Figure A: Effect of Cocoa Procyanidin Fractions on Macrophage  
NO Production



Cocoa Procyanidin Fractions

FIG.13

Figure B: Effect of Cocoa Procyanidin Fractions on LPS Induced  
and  $\gamma$ -Interferon Primed Macrophages



Cocoa Procyanidin Fractions

FIG.14



FIG.15A

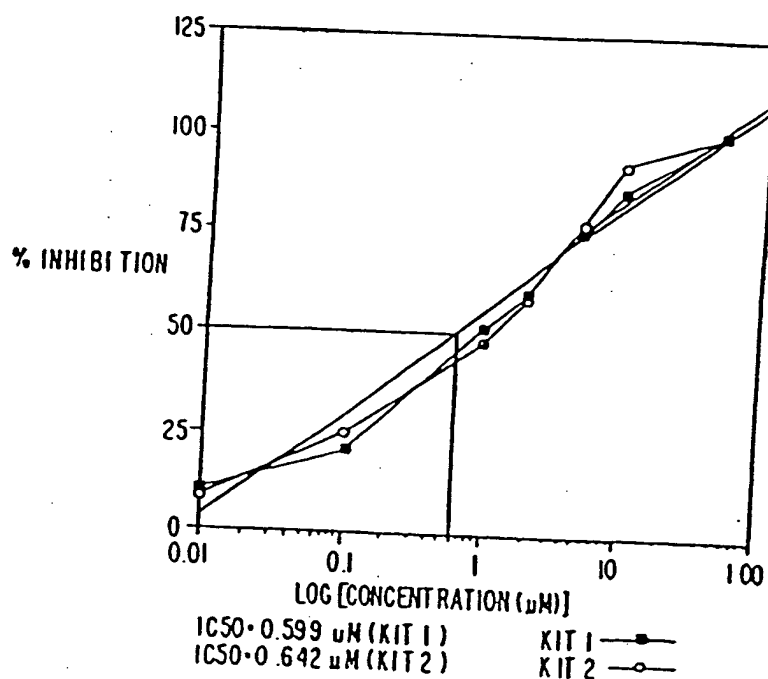
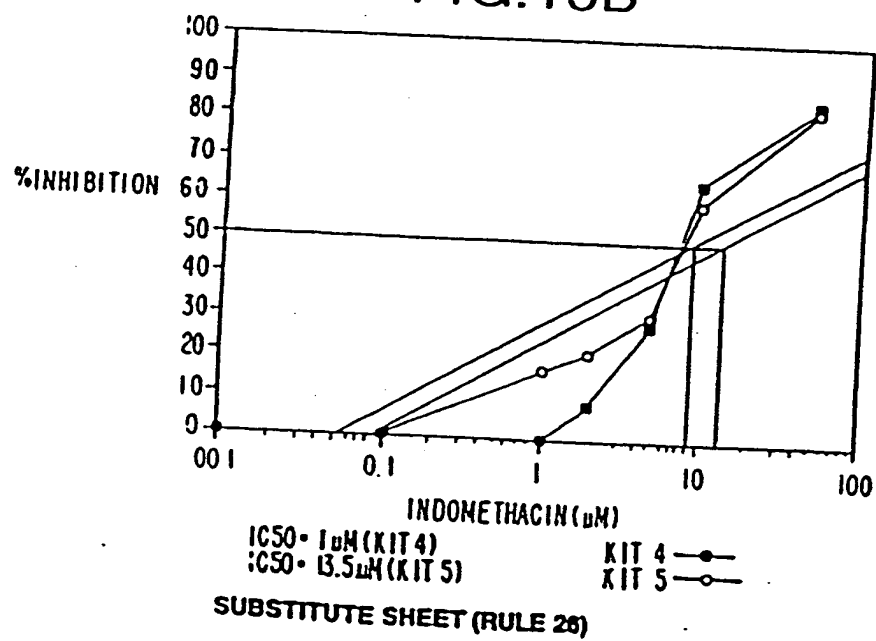


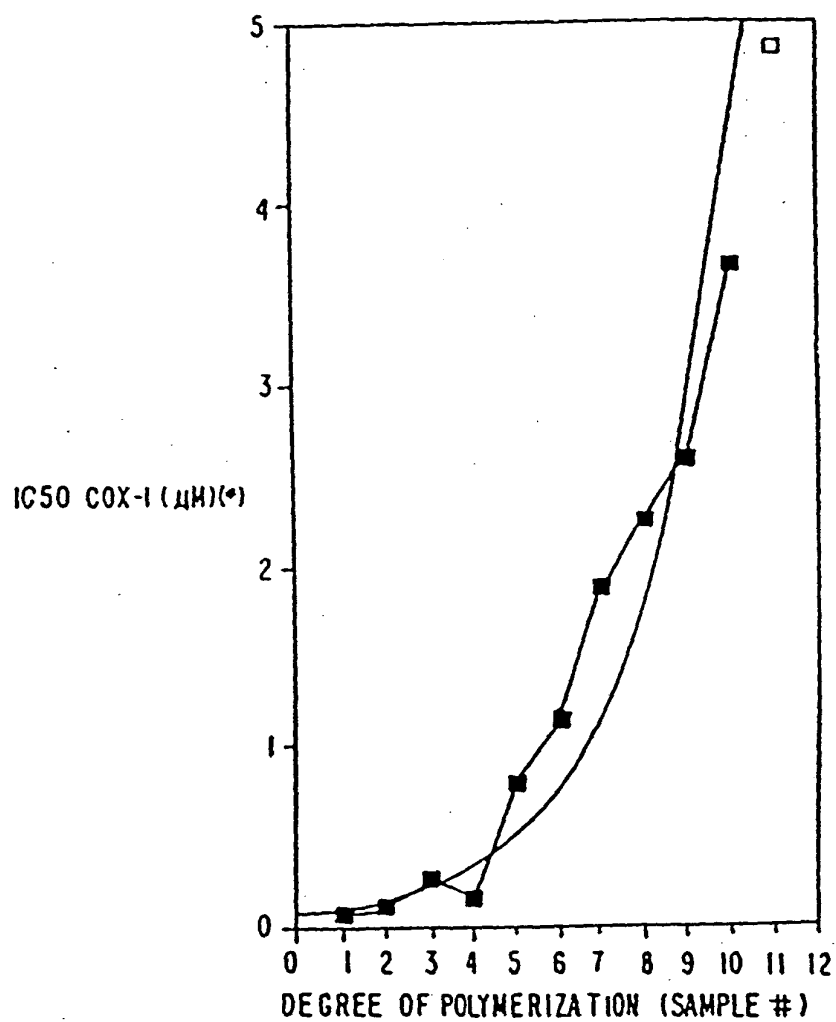
FIG.15B



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FIG.16A



(\*) WITH THE EXCEPTION OF SAMPLE SII EXPRESSED AS mg/ml



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FIG.16B

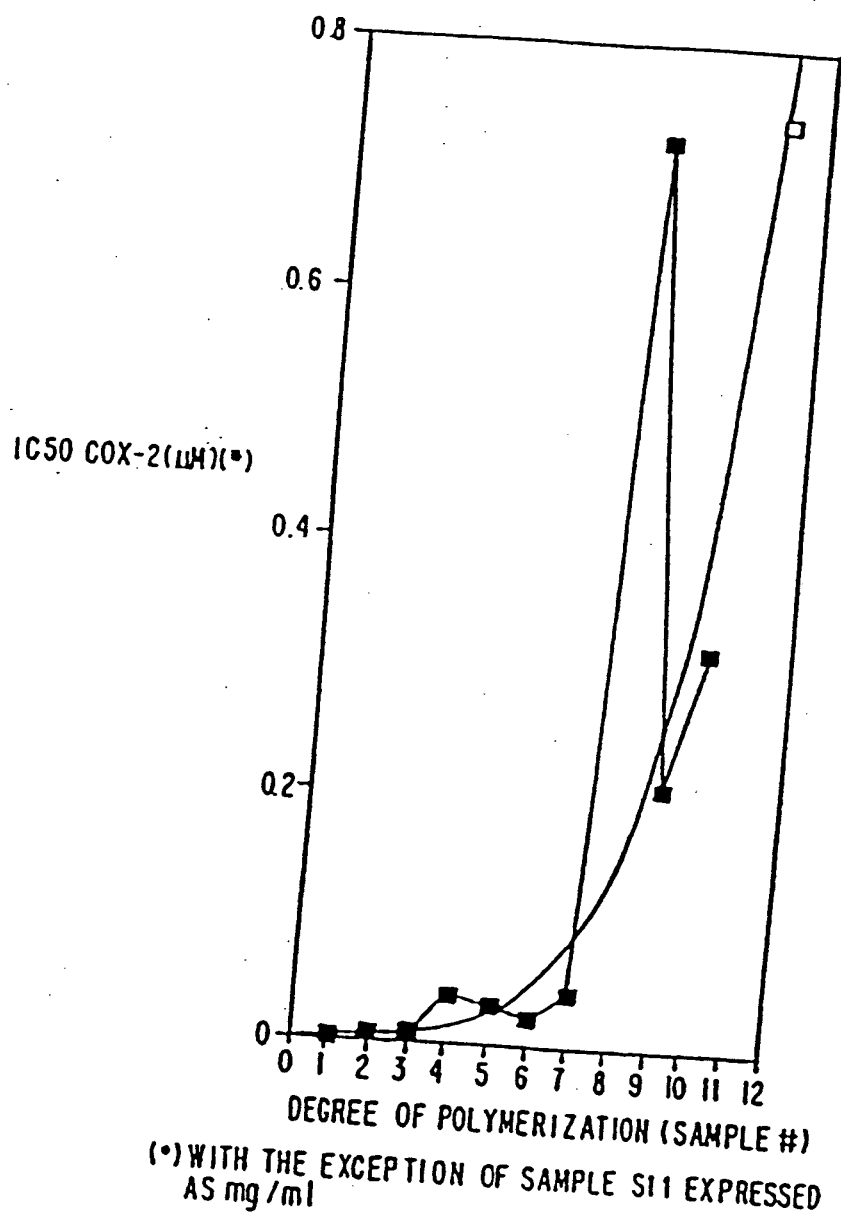
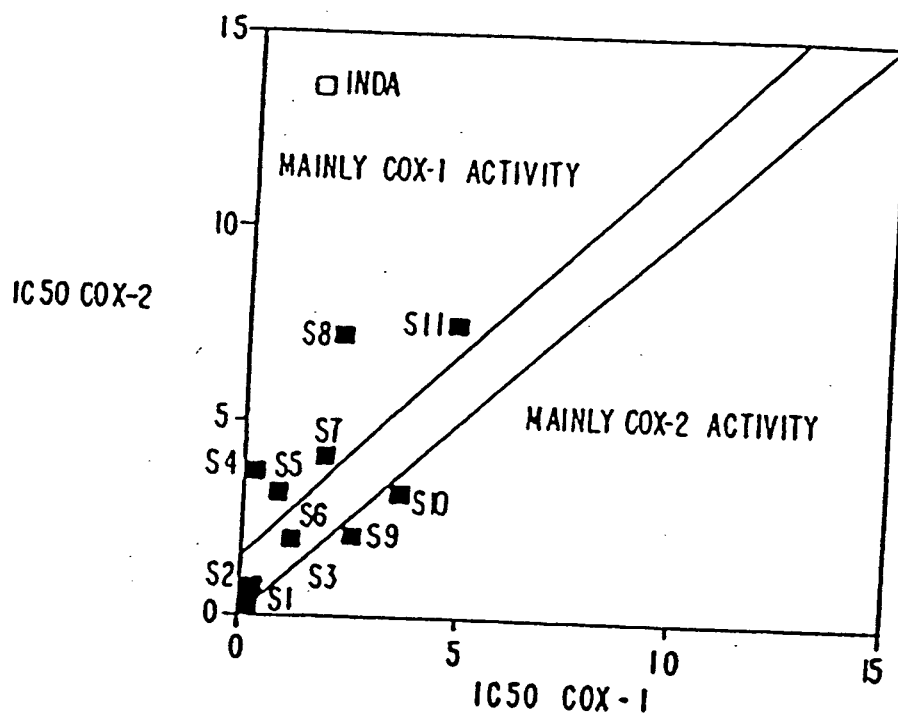




FIG.17



(\*) WITH THE EXEPTION OF SAMPLE S11

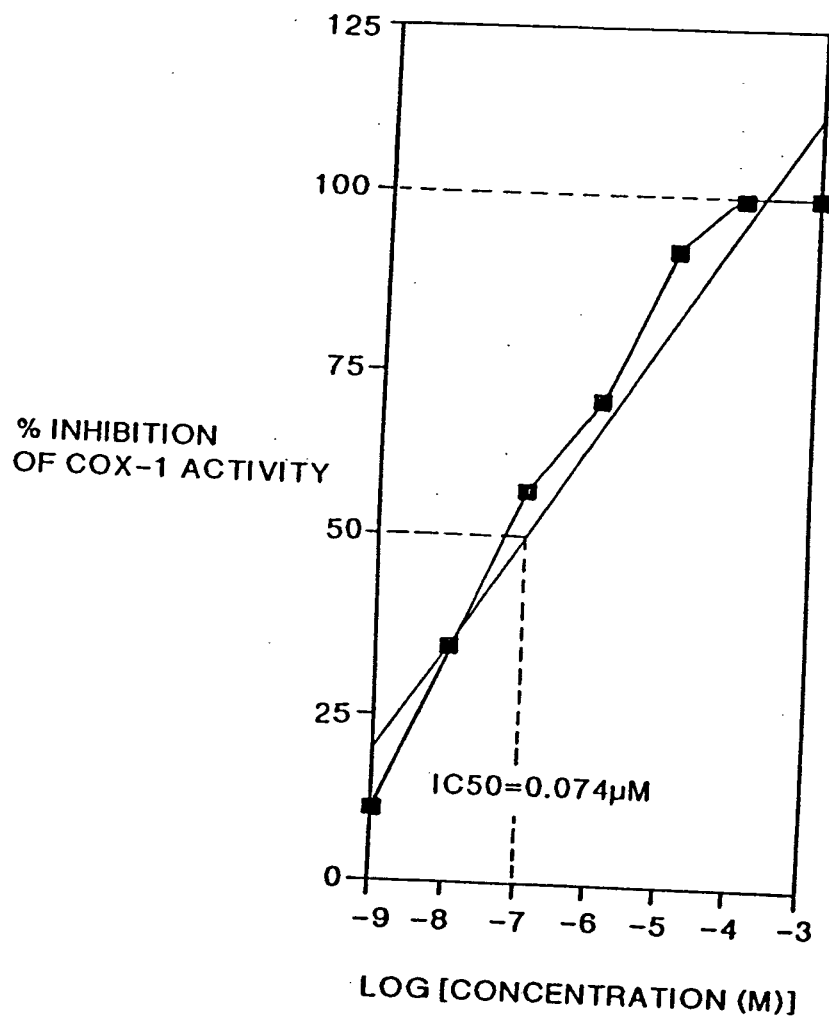


FIG.18A

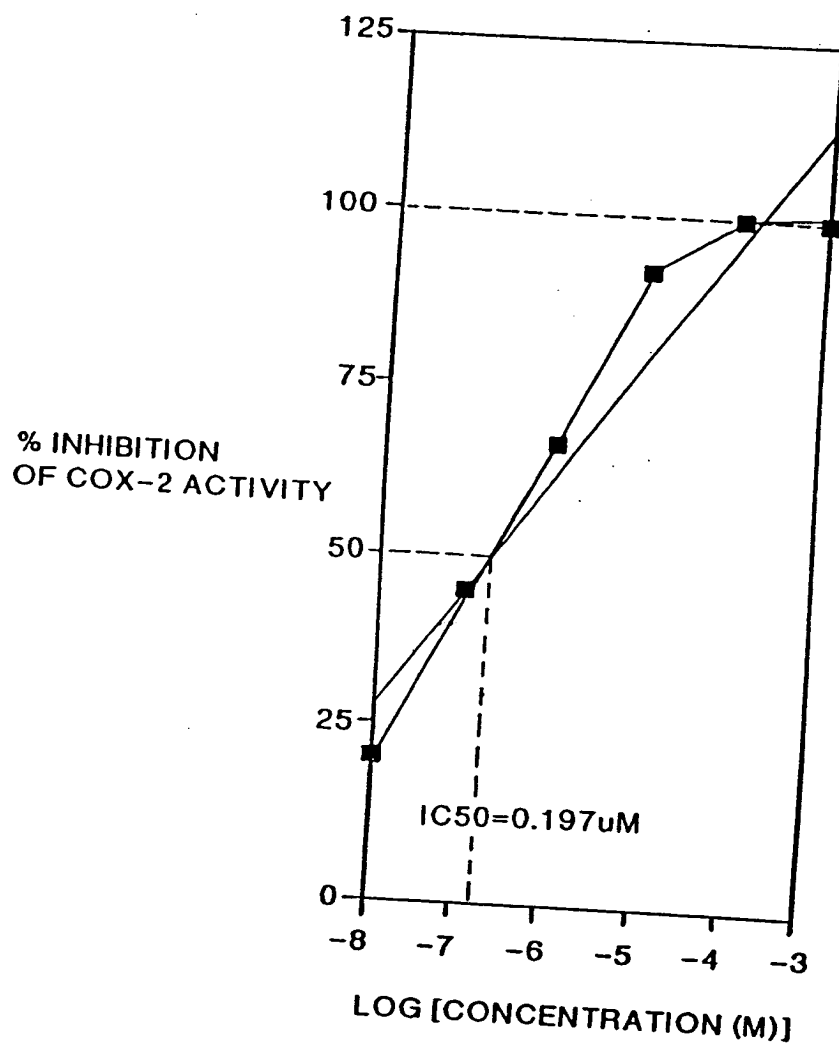


FIG.18B

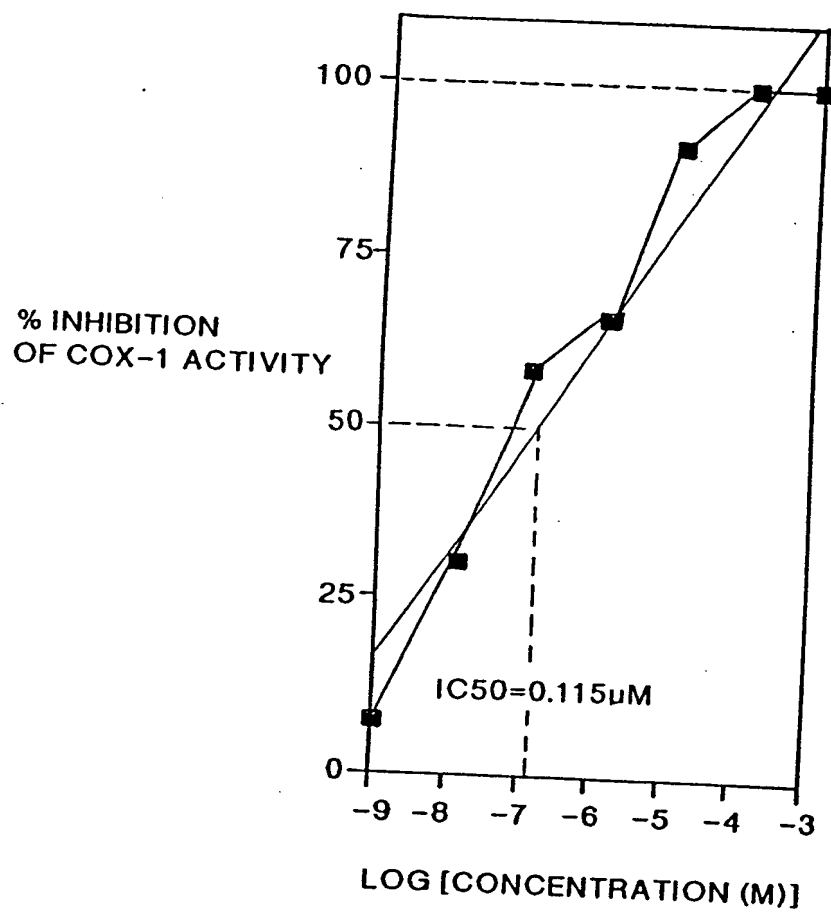


FIG.18C

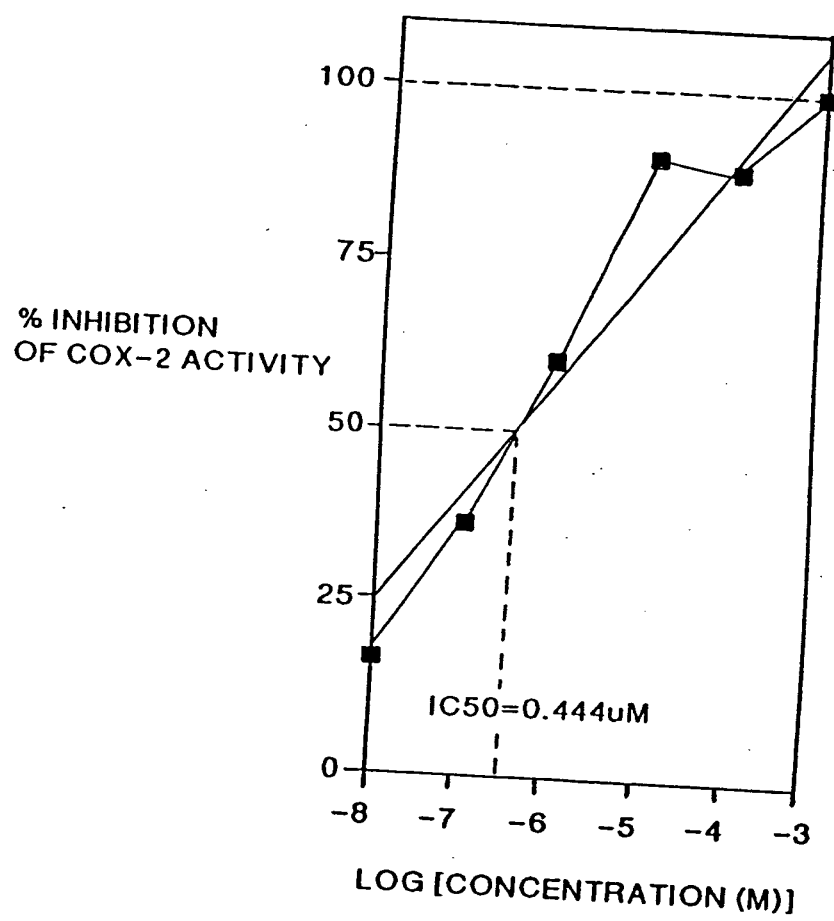
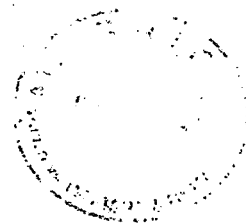


FIG.18D

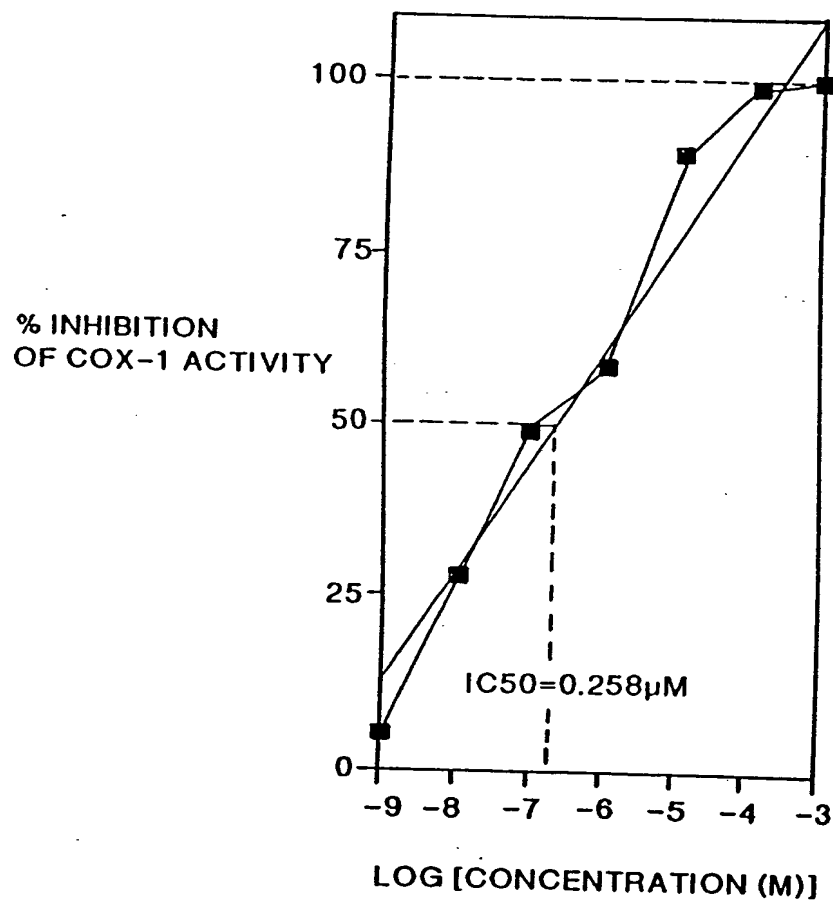


FIG.18E

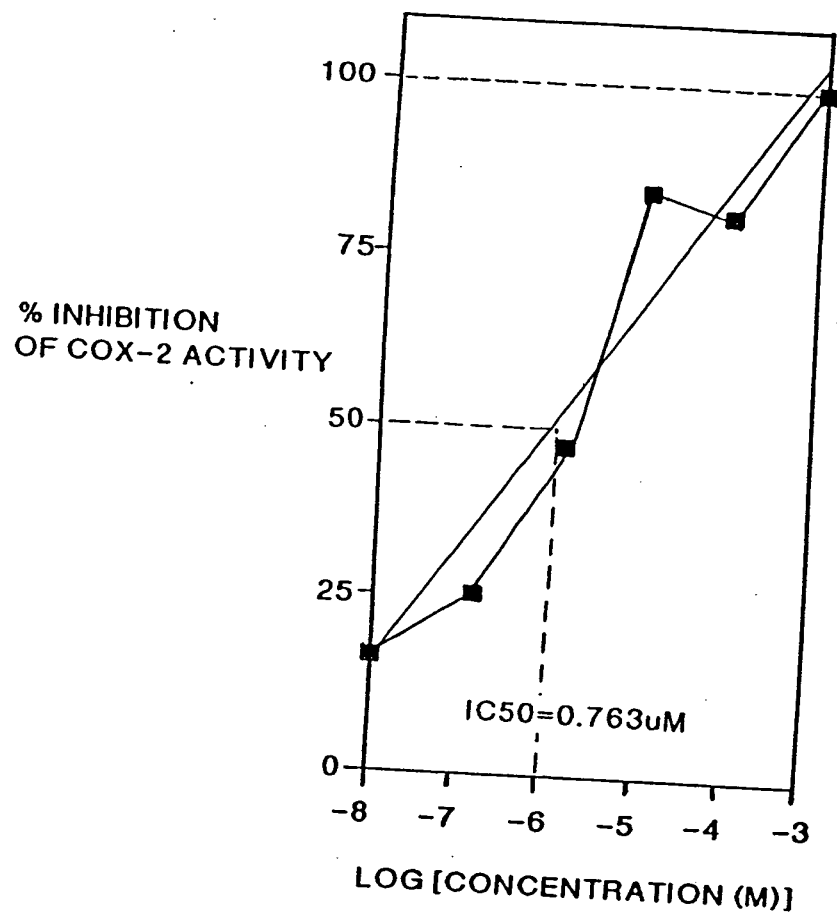


FIG.18F



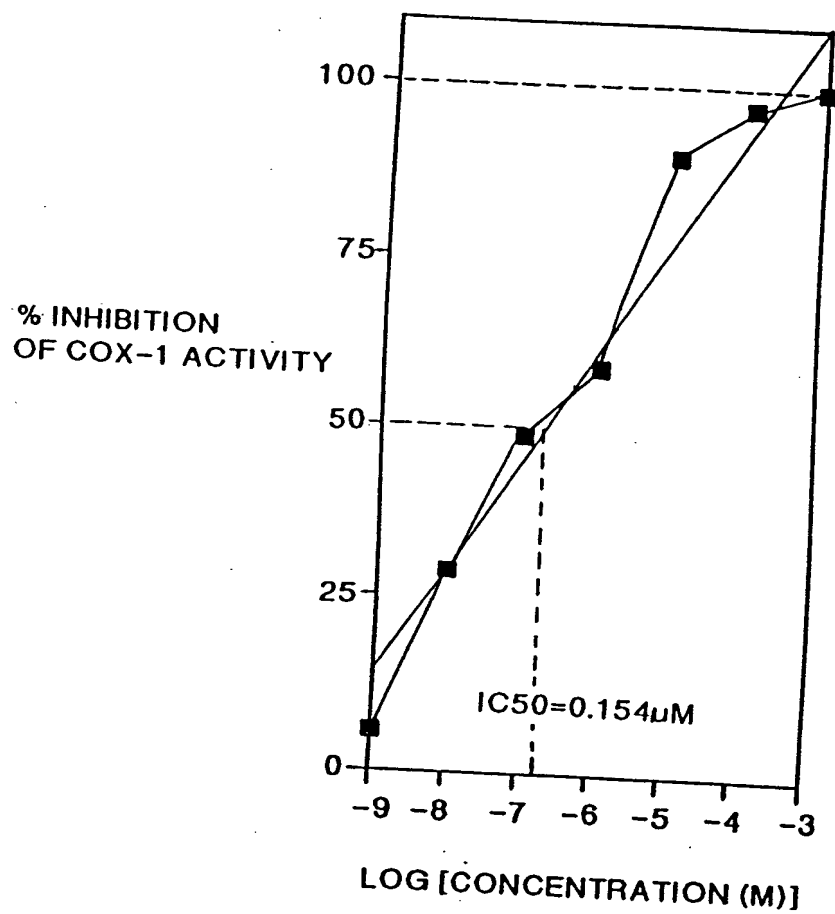


FIG.18G

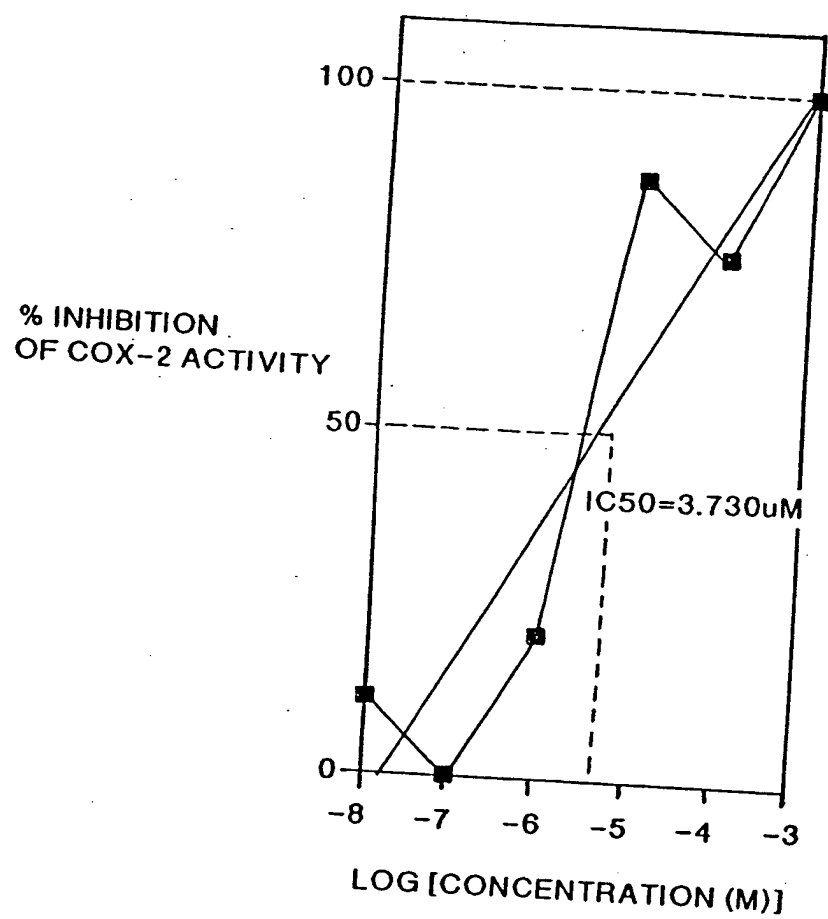
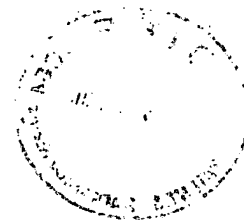


FIG.18H

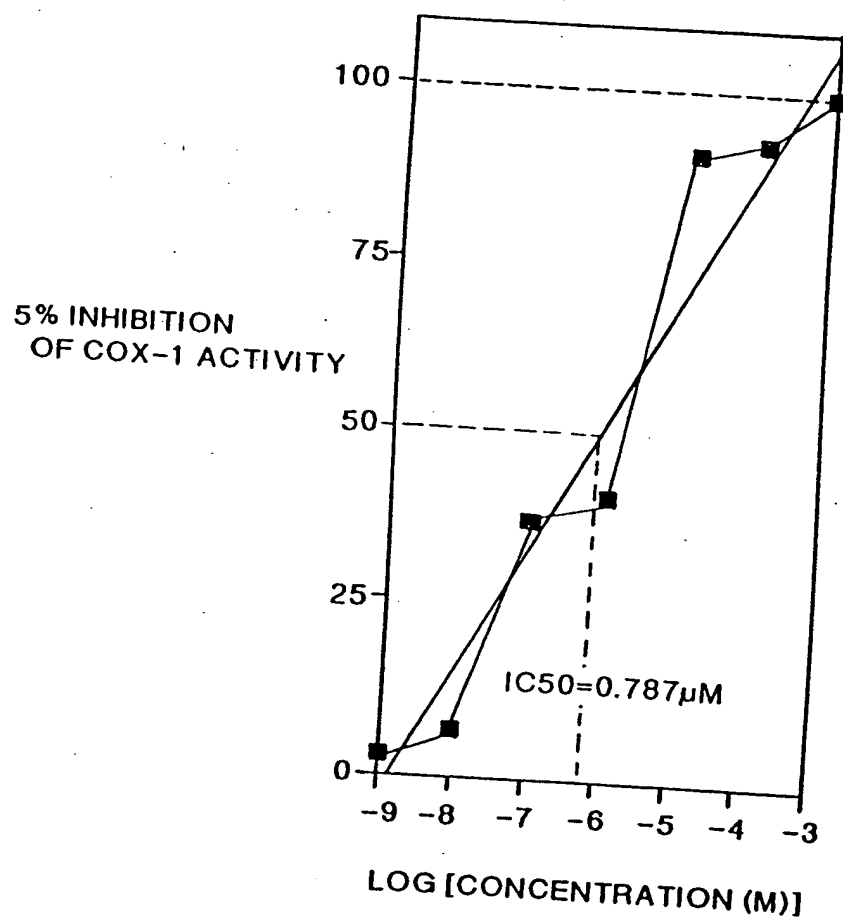


FIG.18 I

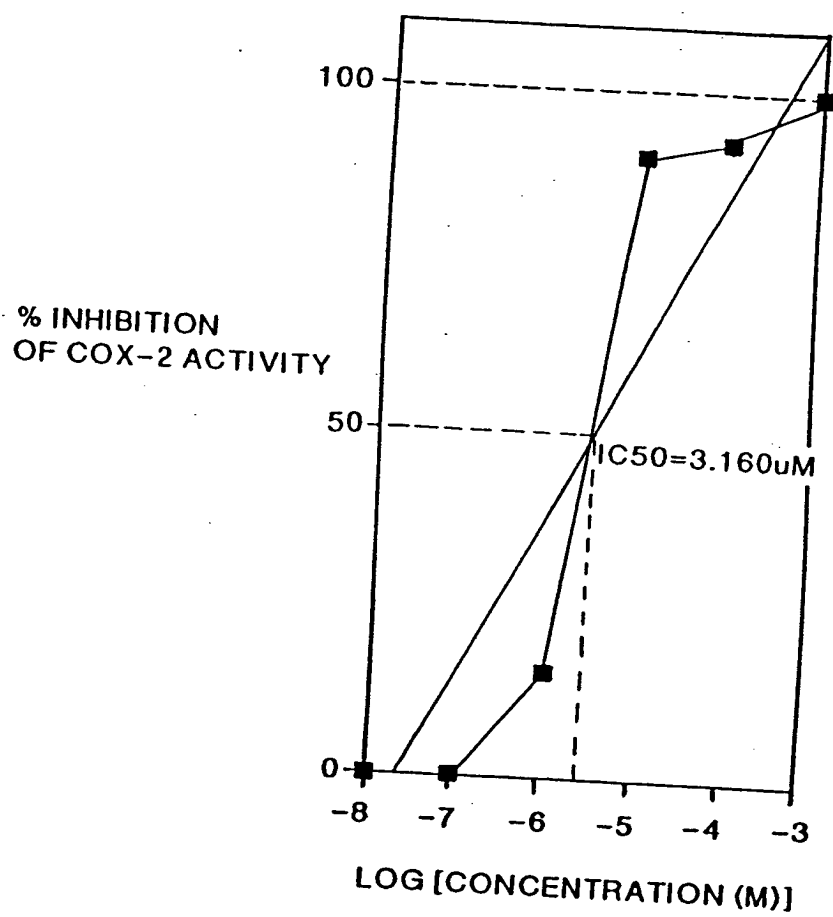


FIG.18J

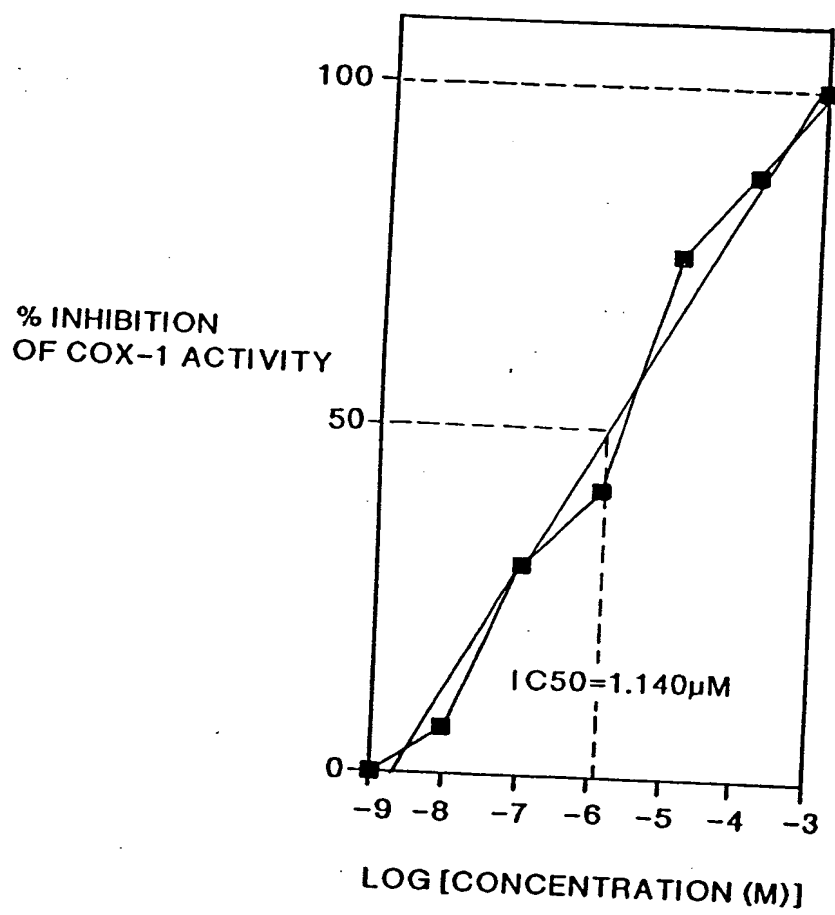
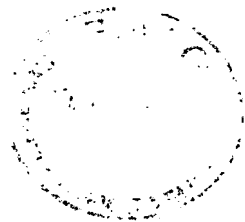


FIG.18K

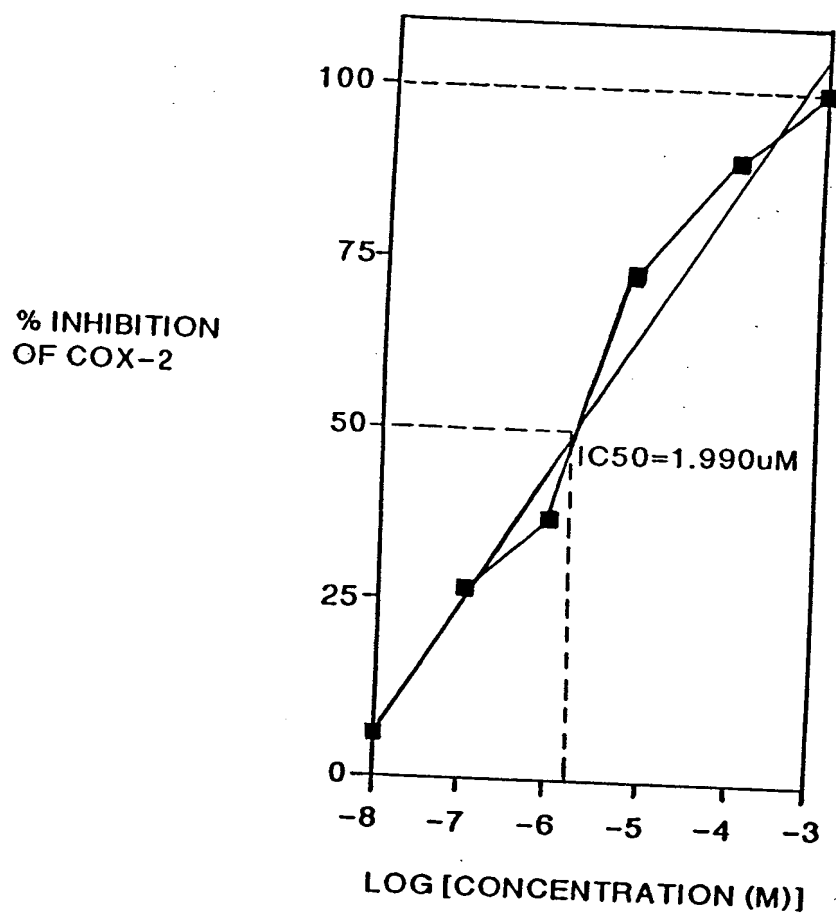


FIG.18L

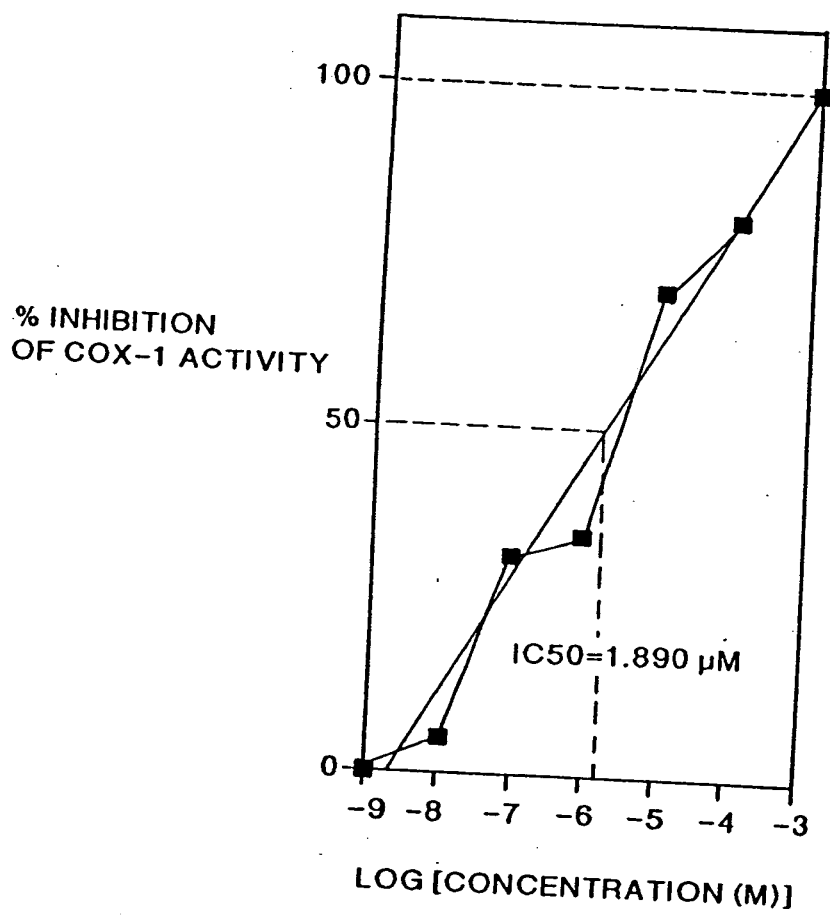


FIG.18M

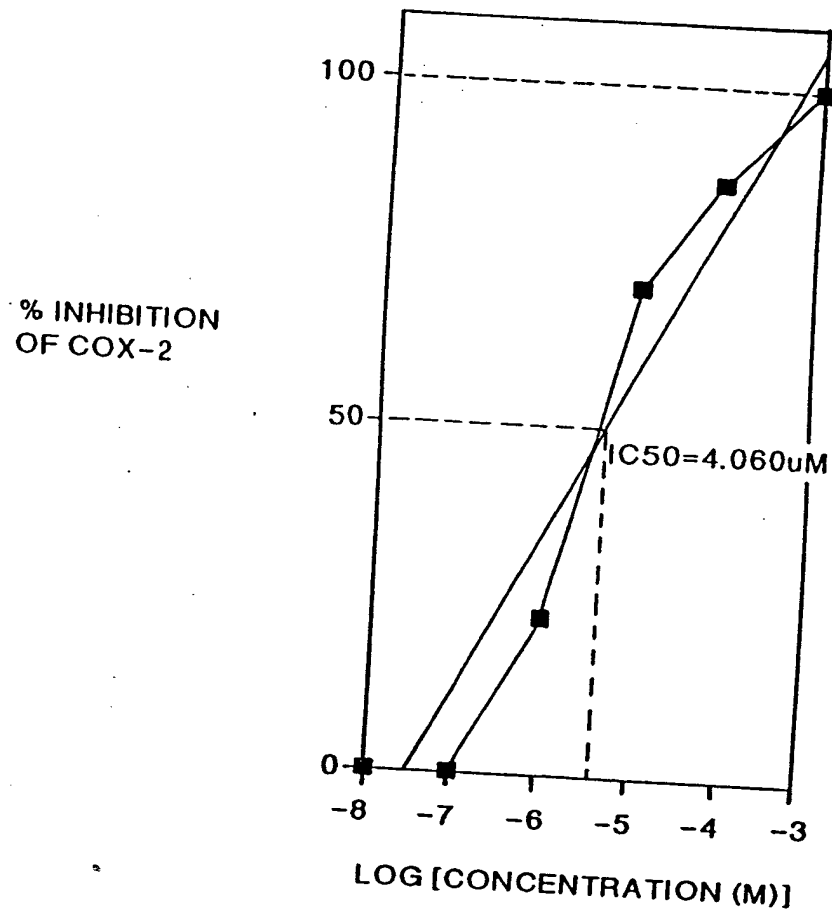


FIG.18N



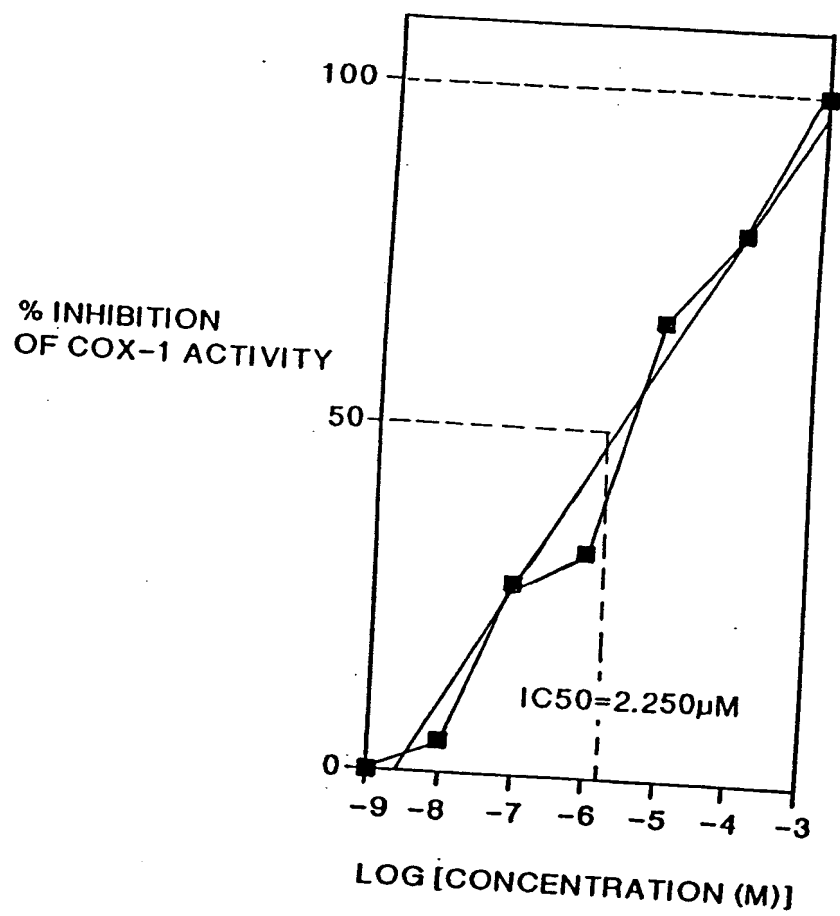


FIG.180



% INHIBITION  
OF COX-2

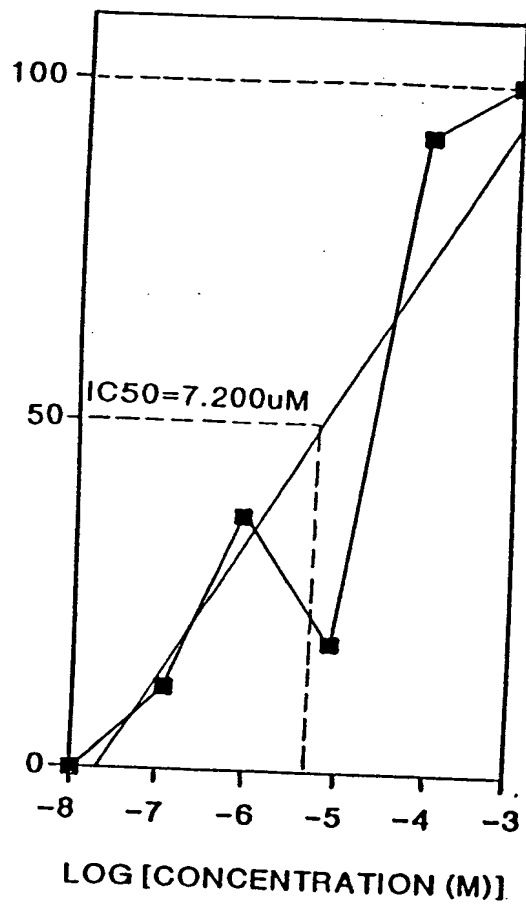


FIG.18P

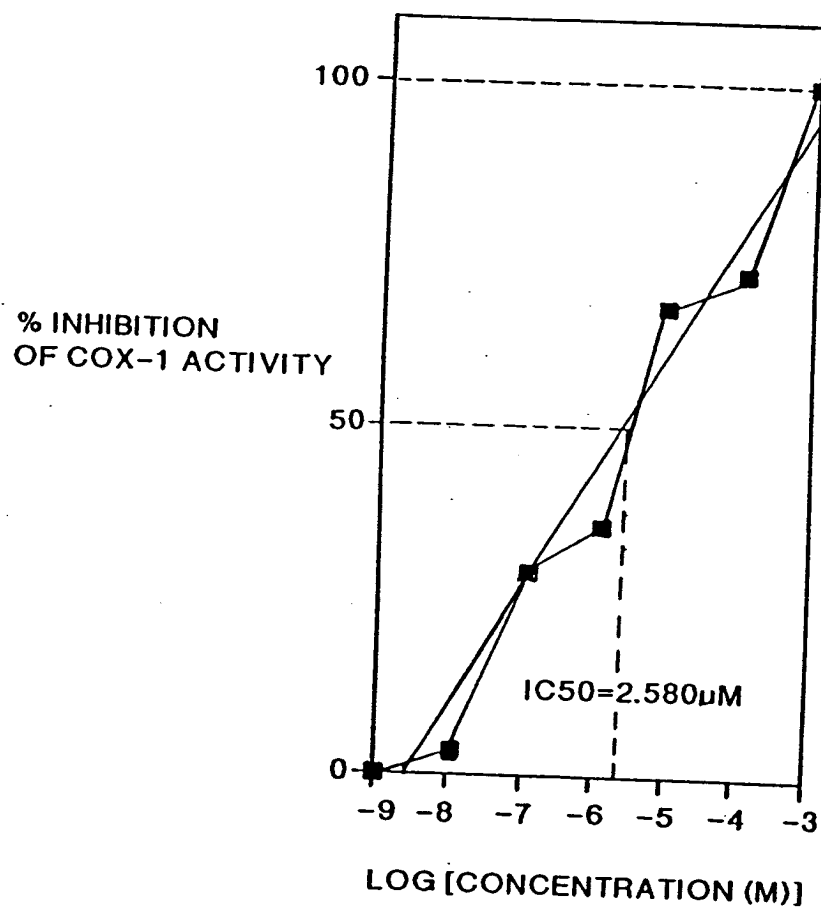
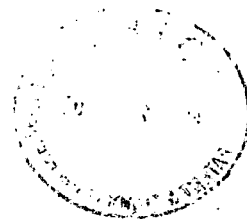


FIG.18Q



% INHIBITION  
OF COX-2

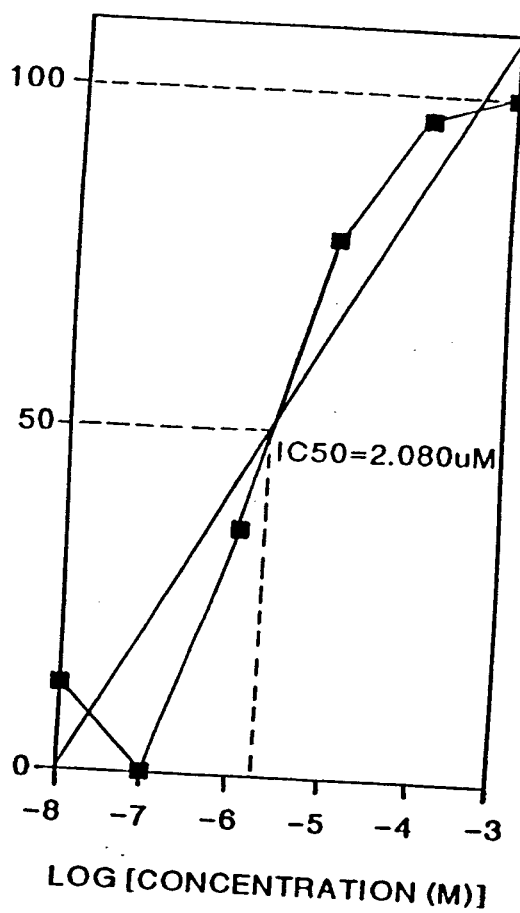


FIG.18 R

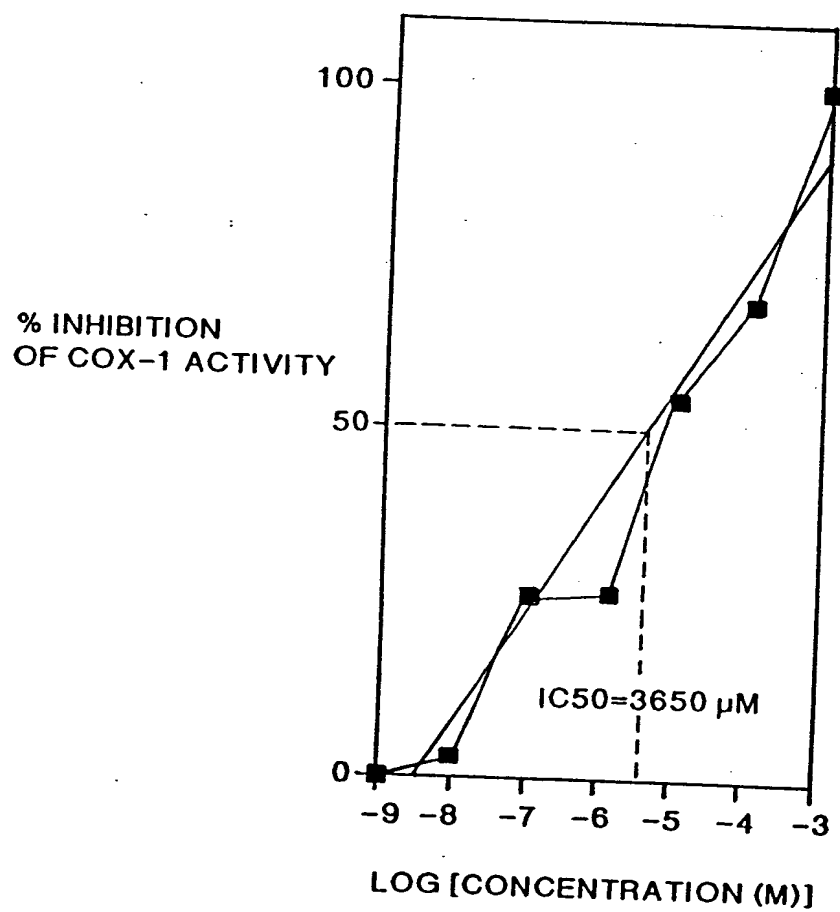


FIG.18S

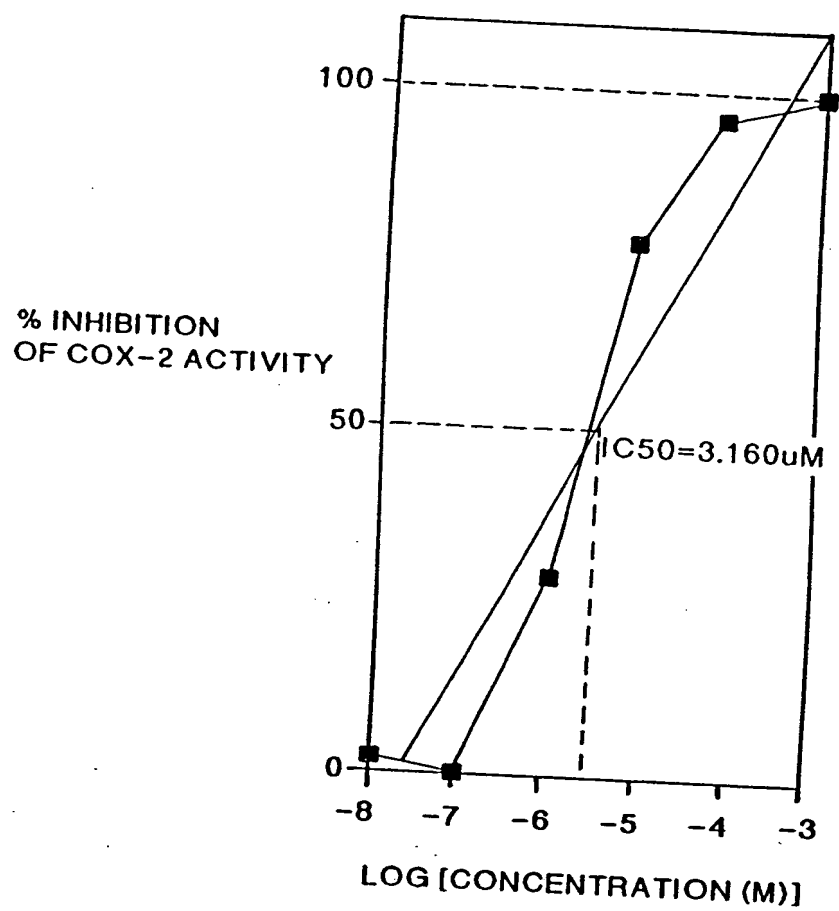


FIG.18T

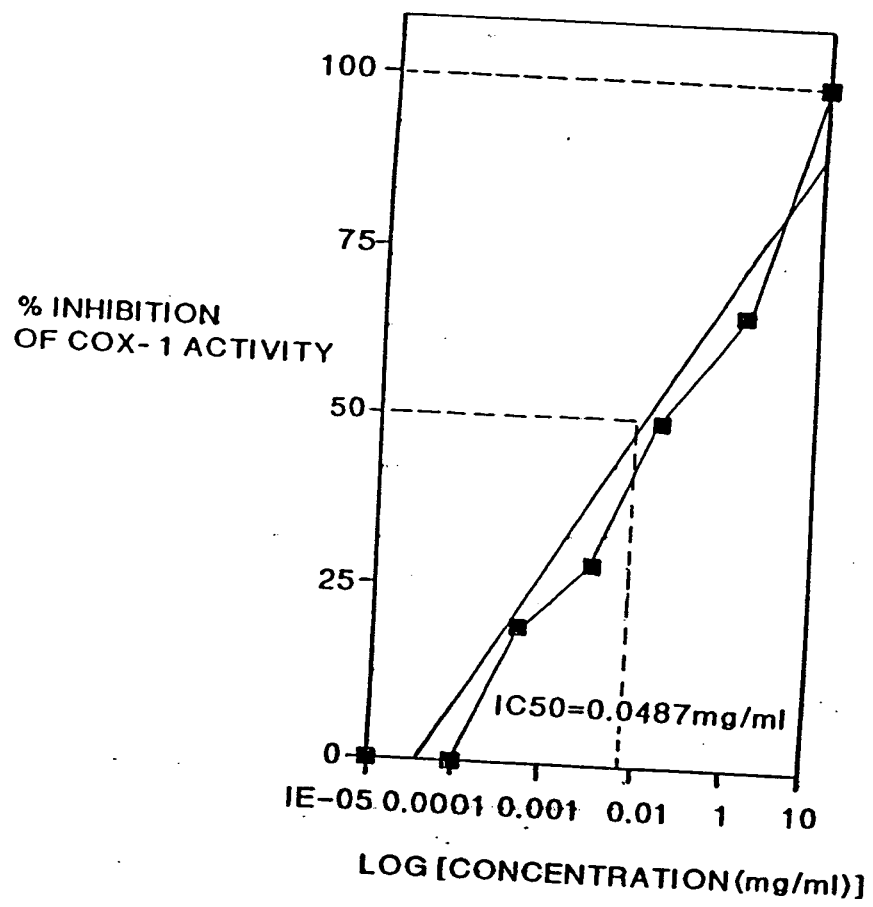


FIG.18U

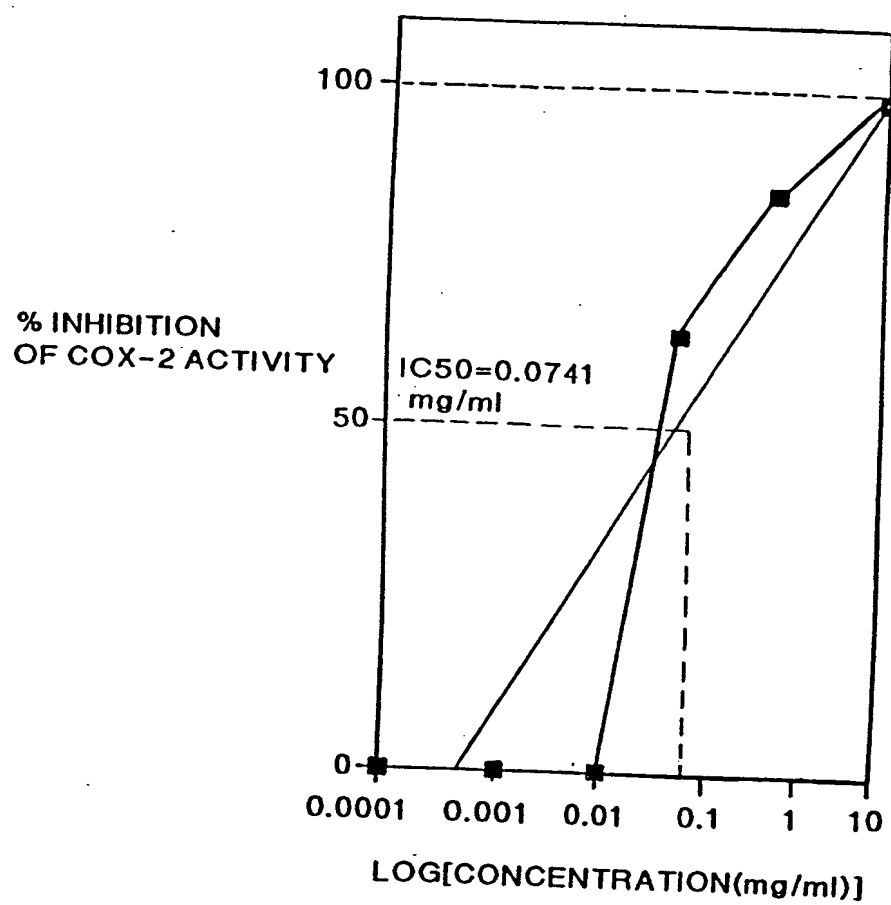
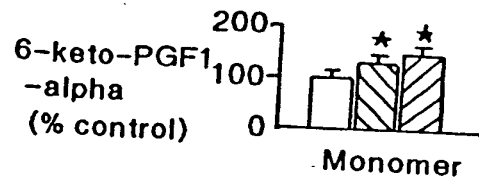
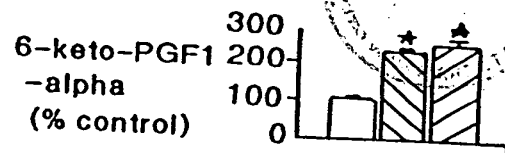


FIG.18V



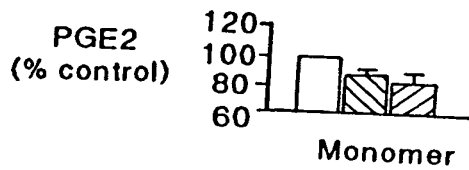


10uM 20uM 30uM

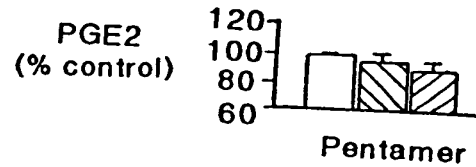


10uM 20uM 30uM

FIG.19A

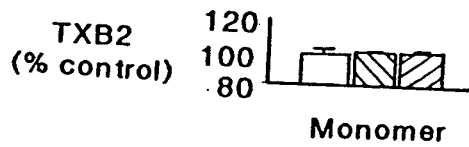


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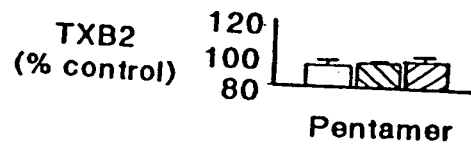


10uM 20uM 30uM

FIG.19B

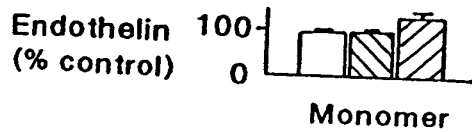


10uM 20uM 30uM

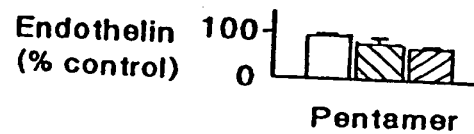


10uM 20uM 30uM

FIG.19C



10uM 20uM 30uM



10uM 20uM 30uM

FIG.19D

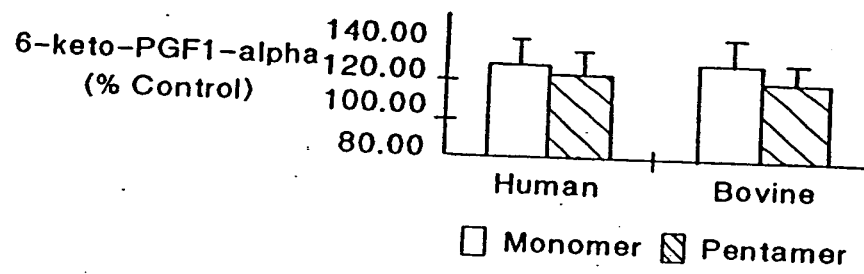


FIG.20A

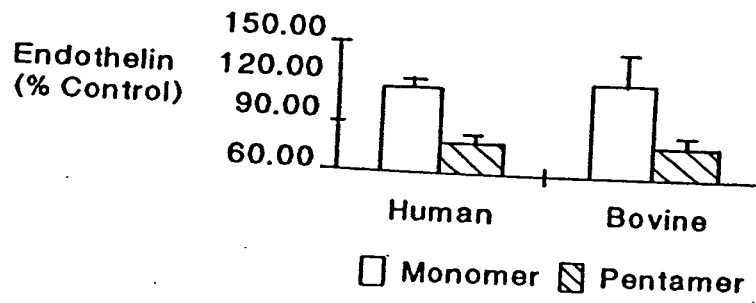
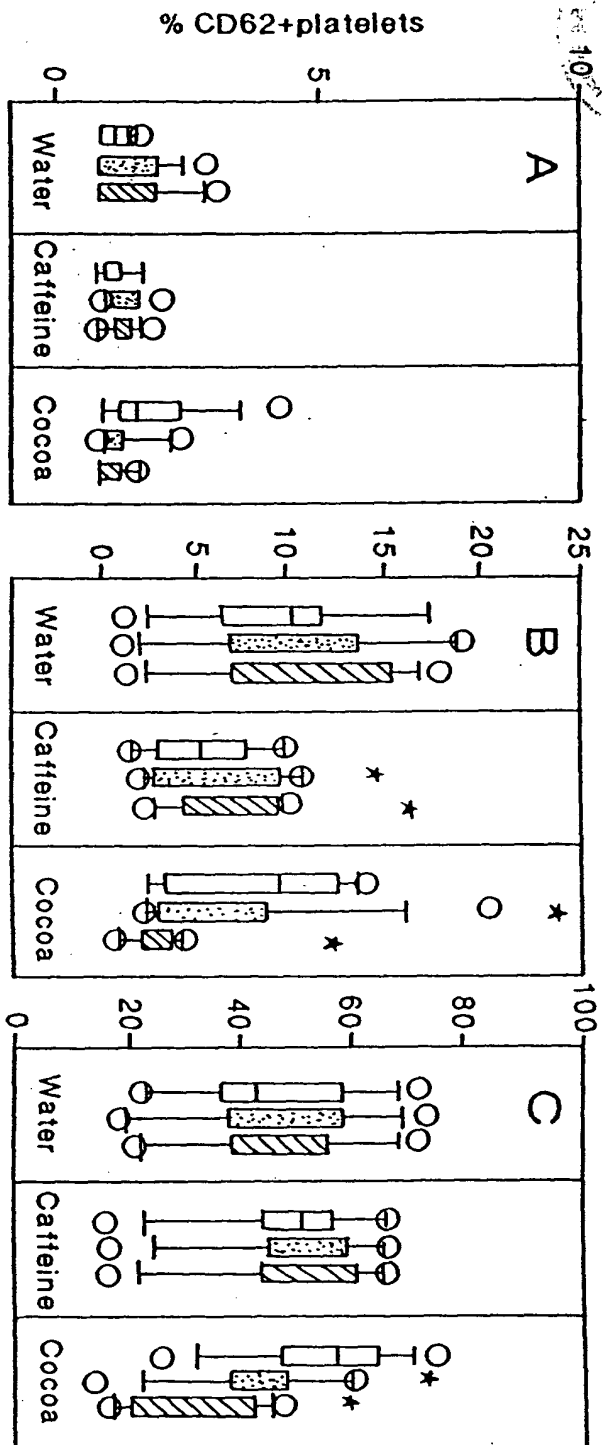


FIG.20B

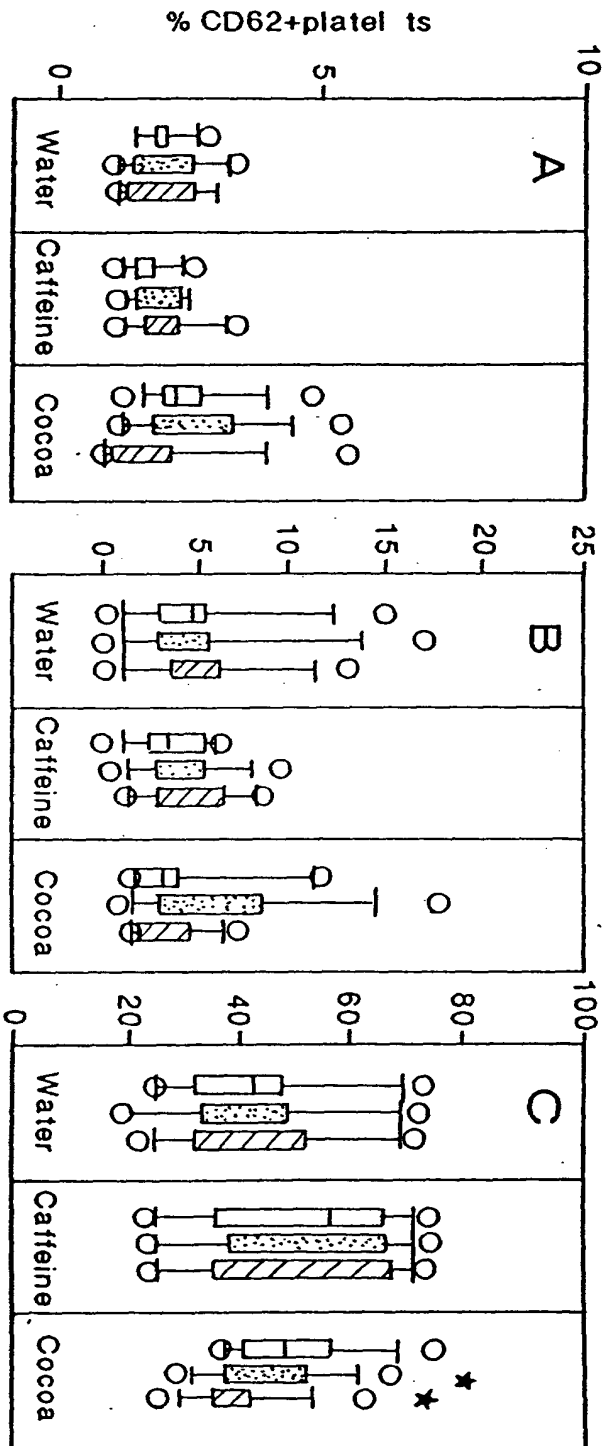
FIG.21



Effect of cocoa beverage consumption on platelet surface expression of activated GP11b-111a with and without stimulation with weak agonists. Platelet activation marker expression is presented as Tukey box plots at times zero (white boxes), 2 hours (light grey boxes), and 6 hours (dark grey boxes) post consumption of water, a caffeine-containing control beverage (caffeine) or a cocoa beverage (cocoa). (A) percentage of platelets expressing activated gp11b-111a (PAC1 = platelets) without stimulation (B) after stimulation with epinephrine (20uM) or (C) with ADP (20uM). Activated GP11b-111a is expressed on the surface of activated platelets. Each box shows the 25-75th percentile, the horizontal bar in the box shows the median. The lines outside the box show the 10th and 90th percentile. Asterisks indicate P 0.05 between zero time and 6 hour time points of each respective data set repeated measure ANOVA on ranks, Student-Newman-Keuls multiple comparison method, n=10 in each



FIG.22



Effect of cocoa beverage consumption on platelet surface expression of activated P-selection with a without stimulation with weak agonists. platelet activation marker expression presented as Tukey box plots at tin zero (white boxes), 2 hours (light grey boxes) and 6 hours (dark grey boxes) post-consumption of water, a caffeine-containing control beverage (caffeine) or a cocoa beverage (cocoa). (A) Percentage of platelets expres P-selection (CD62P+platelets) without stimulation, (P) after stimulation with epinephrine (20uM) or (C) with ADP (20uM). P-selection is expressed on the surface of activated Asterisks indicate  $P < 0.05$  between zero time a hours and between zero time and six